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ASSOCIATE TRAINING PROGRAMS

IN THE

Medical and Biological Sciences

at the

National Institutes of Health

1970 CATALOG

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1970 SCHEDULE FOR APPOINTMENTS TO BEGIN JULY 1, 1972

April 15	Deadline for receipt at NIH of completed applications.
June 8 to 19	Interview period at NIH campus, Bethesda, Maryland (by invitation only).
July 7 to 17	Notification to applicants.

FOREWORD

The National Institutes of Health conducts and supports research to find better ways of preventing or curing disease and lengthening life. In pursuit of that mission, NIH provides broad support for biomedical research, research training, and construction of research facilities in the Nation's medical and dental schools, universities, and other research centers. This is the NIH extramural program.

NIH conducts laboratory and clinical research in its own facilities on its 306-acre campus in Bethesda, Md. For example, in the past year, over 4,000 patients were admitted for investigative studies in the Clinical Center—a research hospital with 516 patient beds and 1,100 laboratories. At any point in time, more than 1,400 research projects are in progress here on the Bethesda campus and at field offices directed from here. This is the NIH intramural program.

Of the 2,210 NIH staff members with doctorates, more than 1,100 have M.D. degrees, 750 have Ph. D. degrees, and some have both. Fifty are dentists, 40 are veterinarians. These individuals with their 3,600 scientifically trained assistants, represent most of the disciplines that contribute to new medical knowledge.

In this scientific community, many opportunities for professional development are available to physicians and others who are undertaking careers in medical or related research, or in academic medicine. The purpose of this catalog is to set forth in one place brief descriptions of programs of concern to those interested in Associateships at the NIH.

ROGER L. BLACK, M.D.,
Associate Director, Clinical Center
Chief, Clinical and Professional Education.

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PART ONE

General Characteristics of Associateships

UNUSUAL opportunities for training and experience in clinical and laboratory investigation are available to physicians and dentists who receive appointments as Clinical, Research, and Staff Associates at the National Institutes of Health. These positions provide broad opportunities for career development in most of the health specialties as well as the basic science disciplines.

Physicians selected for the NIH Associate Program serve on active duty at the National Institutes of Health after completion of residency training (usually 1 year) for which they receive deferment through the PHS CORD Program. A few appointments are also available for immediate active duty following internship.

With respect to dentists, preference for appointment is given to those who have completed 1 year of internship, or possess equivalent advanced training beyond their dental degree. Selection will usually be made 1 year prior to the effective date of appointment. Thus, for example, senior dental students who will enter an accredited internship July 1, 1970, are eligible to apply for an appointment commencing in 1971. Dentists are not eligible for the CORD program.

Although appointments are not limited to those who qualify for the Commissioned Corps of the PHS, Associates usually enter NIH as commissioned officers. For young men who have no fulfilled their military obligation under Selective Service, this obligation can be discharged as Commissioned Officers of the PHS. The residency deferment program for physicians and the responsibilities of a PHS officer are explained in Part Two of this publication.

Appointees are designated as Clinical Associates, Dental Clinical Associates, Research Associates, and Staff Associates. Each Associate is assigned to a preceptor under whose direction he participates in a research program. This represents the most important part of his training experience.

The preceptors are staff members who give generously of their time to help the Associate—not only in relation to research problems under investigation, but in any way they can to enrich the experience of the Associate during his stay at NIH. The levels of research responsibility and latitude given to an Associate depend upon his training and experience as well as his interests and initiative.

Separate didactic exercises are designed to complement Clinical and Research Associateships, but Associates in all four categories are welcome to attend any of the exercises which can accommodate them if their schedules permit. In addition, postgraduate instruction is available through evening courses offered by the Foundation for Advanced Education in the Sciences, Inc. (see Part Four), and Associates in many program areas are expected to take advantage of this academic opportunity.

Associateship appointments are generally made for 2 years; in certain Institutes, appointments may be extended for an additional year. Unless he seeks transfer to another area of the Public Health Service, an Associate may expect to end his active duty as an officer at the completion of his Associateship appointment.

The Clinical Associate

The Clinical Associate participates in both clinical and laboratory research. Institute programs differ in the proportion of time devoted to laboratory and clinical responsibilities.

Ward activities are under immediate supervision of competent clinical investigators, and include a wide variety of rounds, conferences, and other instructive exercises. Proximity to the patient's bedside of collaborating scientists from many biological disciplines has created an unusual opportunity for clinical investigation at the NIH Clinical Center.

Clinical Associates are not in formal residency training programs, even though they may be performing many of the same functions that residents do in other hospitals. Some Associates appointed to Dermatology, Neurology, and Psychiatry programs are recommended for a limited amount of residency credit by their respective program chiefs. Associates in positions providing further training in Internal Medicine who remain at NIH for a third year may receive credit for this year upon application to the American Board of Internal Medicine.

The Dental Clinical Associate

Like his physician Clinical Associate counterpart, the Dental Clinical Associate may participate in laboratory and clinical research, while at the same time enhancing his professional skills by providing treatment to the research patient pool serviced by the Dental Clinic at NIH.

During the 2-year tenure of the Associateship, full opportunity is provided for: (1) familiarization with all ongoing research programs of relevance to dentistry; (2) affiliation, in a preceptor-preceptee relationship, with one or more program leaders, so as to allow meaningful participation in a mutually acceptable area of investigation; and (3) extension of scientific background through rounds, conferences, seminars and formalized course work. (See p. 47) for a more complete description of the research programs of the National Institute of Dental Research.)

The Research Associate

The Research Associate devotes the larger portion of his time to laboratory research in the biomedical sciences. His preceptor is responsible for training him in research methodology and design, and for guiding him in the conduct of specific research undertakings and in the interpretation of results. A real effort is made to select research problems which will enable the Associate to gain breadth and perspective, encounter a variety of laboratory problems, and learn many different approaches rather than become a specialist in one or two refined techniques.

In addition, the Research Associate participates in a series of formal tutorial seminars and informal discussion groups designed in content and emphasis for prospective independent investigators. This program is designed to furnish the training in basic medical sciences normally received by Ph. D. candidates but not generally by candidates for the M.D. degree.

The Pharmacology Research Associate

Through an expansion of the NIH Associate Training Program, the National Institutes of Health is increasing its commitment to develop scientific manpower for both basic and applied research in pharmacology and closely related areas of biomedical science.

The Pharmacology Research Associate devotes the larger portion of his time to laboratory research. He receives intensive research training in a number of disciplines related to modern pharmacology. He also attends formal teaching seminars and informal discussion groups which will provide him with the opportunity to master selected topics perhaps not adequately covered during his academic training.

The Staff Associate

The Staff Associate position provides opportunities for those highly qualified candidates who could contribute significantly to research in areas which are not specifically designated in the Research or Clinical Associate categories. The Staff Associate may participate in either laboratory or clinical research or both, depending upon the activities of the senior investigator with whom he works. Research experience may be supplemented by formal evening study courses, as well as by attendance at lectures by guest speakers and a variety of regularly scheduled seminars.

PART TWO

Applying for an Associateship

Approximately 100 Clinical Associates and 50 Research and Staff Associates are appointed annually, usually as commissioned officers. In special cases, appointment may be considered under the Civil Service mechanism. Of course, in such instances, the following statements relating to the PHS Commissioned Corps, the commissioning process and the CORD Program would not apply.

To be considered for a Clinical, Research, or Staff Associate appointment, an applicant must submit the following forms properly executed no later than April 15, 1970, to the Chief, Clinical and Professional Education, National Institutes of Health, Bethesda, Md. 20014:

- Information Record for Clinical, Research, and Staff Associate positions;
- Program Area Selection Check List;
- NIH Associate Information and Status Record;
- Interview Information Record;
- Application for Appointment as a Commissioned Officer in the U.S. Public Health Service (2 copies);
- Fingerprint chart (fingerprints may be obtained at PHS facilities or through the local police or post office).

The applicant is responsible for requesting the following materials, which must be received by April 15 to complete the application:

- Three sets of references from professional persons whom the candidate has listed on the NIH information sheet (each set consists of: (1) Request for confidential evaluation of applicant for appointment as an NIH Associate; and (2) Reference Request (Commissioned Corps).
- Two copies of all college and medical or dental school transcripts (showing class standing, if available).

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A candidate's application for a commission in the Public Health Service does not commit him to accept a commission in the event he is not selected for an Associate position at NIH. However, there are many splendid alternative opportunities for physicians and dentists in the Public Health Service which may appeal to such a candidate, and this commission application would be usable for such appointments.

The U.S. Public Health Service does not discriminate in employment because of an applicant's race, color, or national origin.

Commissioned Officer Residency Deferment Program

The Commissioned Officer Residency Deferment Program (CORD), developed and conducted by the U.S. Public Health Service with the cooperation of the Selective Service System, permits a limited number of draft-eligible physicians (1) to become Inactive Reserve officers in the Commissioned Corps of the Public Health Service and (2) to complete 1 or more years of formal residency training before serving on active duty. Dentists are ineligible for the CORD Program.

CORD Program participants are appointed commissioned officers in the Inactive Reserve of the Public Health Service. They do not receive pay from the Service until called to active duty. The stipend normally paid by the hospital to residents may be accepted by CORD Program officers.

In addition to being fully qualified for active duty in the Commissioned Corps of the Public Health Service, participation in the CORD Program requires that an applicant must:

- Be a citizen of the United States.
- Meet the physical standards of the PHS.
- Satisfactorily complete an internship approved by the Council on Medical Education of the American Medical Association.
- Be a graduate of a medical school approved by the Council on Medical Education of the American Medical Association.
- Be liable for 2 years of service under the general provision of the Military Selective Service Act.
- Pursue *clinical* training which is fully creditable toward fulfillment of minimum residency requirements for certification by an American medical specialty board.

When residency training is completed and/or deferment is terminated, the CORD Program officer is obligated to serve on active duty with the Public Health Service for a period of at least 24 months. This period of service will satisfy Selective Service obligations and no further service is required.

It should be noted that, even though tentatively selected for the CORD Program, an applicant cannot participate unless also found fully qualified for appointment as a commissioned officer.

The questions most frequently asked by CORD Program applicants and participants are answered below:

Q. May I apply simultaneously for the Berry and CORD Programs?

A. Yes.

Q. As an intern in a USPHS hospital (or other uniformed service hospital), am I eligible for the CORD Program?

A. If you are interning as a commissioned officer on active duty in the Army, Navy, Air Force, or Public Health Service, you are not eligible to participate in the CORD Program.

Q. Are participants in the Senior Medical Student Program of the Army (or other service) eligible for the CORD Program?

A. No.

Q. As a CORD participant, may I be deferred for a research fellowship?

A. No. Deferment may not be recommended for periods of basic science or other graduate training unless the academic training is an integral part of a clinical residency program. Such training must be fully creditable toward fulfillment of minimum residency training requirements for certification by an American medical specialty board.

Q. I have applied for the CORD Program. Will the induction notice I recently received from my local Selective Service Board alter my status as a CORD Program applicant?

A. Yes. If you receive an induction notice after applying for the CORD Program, notify the Office of Personnel and Training immediately.

Q. Is there an age limit for the CORD Program?

A. Yes. You must complete CORD Program participation and begin active duty before age 32.

Q. If I am not selected for the NIH Associate Program, may I be considered for deferment under some other PHS activity?

A. Yes. If you apply and are not accepted for an NIH Associate assignment, you may elect (1) to be considered for residency deferment and subsequent active duty in one of the other activities of the Public Health Service, (2) to request active duty, or (3) to withdraw your application for a commission.

Q. I have received notification of selection for CORD Program participation and deferment beginning July 1, 1971. Is it possible for my deferment to begin on February 1?

A. No. Deferment before July 1 cannot be arranged.

Q. I was selected for the CORD Program and residency training in surgery but have now decided I wish to train in pediatrics. May I change my specialty?

A. No. Changes in specialty are not permitted after selections are made.

Q. May I change hospitals while participating in the CORD Program?

A. Yes, provided the new program is approved by the Council on Medical Education of the American Medical Association, all the training is fully creditable by your specialty board, and you notify the Commissioned Personnel Operations Division, Office of Personnel and Training.

Q. Is it possible to withdraw from the program prior to actual deferment?

A. Yes. You may withdraw your CORD Program application at any time prior to appointment as a commissioned officer, or, if you have already been appointed, you may resign the commission.

Q. May I be deferred for graduate training?

A. No, deferment may not be recommended for periods of basic science or other graduate training unless the academic training is an integral part of a clinical residency program and counts toward satisfying minimum board requirements.

Q. For what rank am I eligible?

A. If you enter the CORD Program immediately following internship, you will be appointed in the grade of Assistant Surgeon (Inactive Reserve), which is equivalent to Lieutenant, jg., in the Navy. When called to active duty, you will receive a promotion to the grade of Surgeon (Reserve), which is equivalent to Lieutenant Commander in the Navy.

Method of Selection—Matching Program

Appointments are based upon intellectual attainment and demonstrated research interest and ability. A man's background in research is often a decisive factor in making selections. This applies more significantly in certain areas—such as internal medicine and psychiatry—than in others—such as surgery and radiology.

All applications are carefully considered; but it should be understood that successful candidates have outstanding records in medical or dental school and their references indicate that they have exceptional research training and/or potential.

Associates are selected by a system of matching the candidates' program-area preferences against nominations made by the Institutes (similar to NIMP, Inc.).

In his packet of forms, a candidate will find several sheets, each headed "Program Area Selection Check List." After reading Part Three of this catalog, he should check off on these sheets the areas in which he is interested. He does not indicate his preferences at this point, and he is not limited to any particular number of choices. The check marks that he makes will determine the laboratories and branches to which his application will be circulated at the National Institutes of Health.

After thorough review of all candidates' qualifications by the Institutes, a limited number of candidates will be selected for personal interviews to be held during a 2-week period from June 8 through 19. Candidates should be prepared to come to NIH for an interview on short notice on any date within this period, at their own expense. All interviews are by invitation and will be arranged through the Clinical and Professional Education Office. Following interviews, candidates will be requested to indicate their preferences, which are kept in confidence and used exclusively for matching against the Institutes' nominations. Successful candidates will be notified on July 7 and be given an opportunity to accept or reject the positions for which they were matched.

PART THREE

Program Areas for Which Candidates May Apply

EACH of the major NIH components has prepared a description of its program areas for which Associates may seek appointment. Due to diversity of the operations and programs within these major components, the descriptions do not follow a pattern. In effect, however, all of these descriptions are meant to anticipate the questions which applicants may have in selecting the program areas for which they wish to be considered. It should be noted that a candidate is not limited as to the number or kinds of positions for which he may apply.

National Cancer Institute

Acting Director, Carl G. Baker, M.D.
Clinical Director, Nathaniel I. Berlin, M.D., Ph. D.

Laboratories and Branches

Scientific Director for General Laboratories and Clinics, Nathaniel I. Berlin, M.D., Ph. D.
Acting Chief, Laboratory of Biochemistry, Edward L. Kuff, M.D., Ph. D.
Chief, Laboratory of Biology, Walter E. Heston, Ph. D.
Head, Macromolecular Biology Section, Peter T. Mora, Ph. D.
Chief, Laboratory of Physiology, Julius White, Ph. D.

Acting Chief, Laboratory of Pathology and Pathologic Anatomy Branch, Louis B. Thomas, M.D.
Chief, Dermatology Branch, Marvin A. Lutzner, M.D.
Chief, Endocrine Evaluation Branch, Erwin P. Vollmer, Ph.D.
Chief, Endocrinology Branch, Mortimer B. Lipsett, M.D.
Chief, Immunology Branch, John L. Fahey, M.D.
Chief, Metabolism Branch, Nathaniel I. Berlin, M.D., Ph. D.
Chief, Radiation Branch, Ralph E. Johnson, M.D.
Chief, Surgery Branch, Alfred S. Ketcham, M.D.
Scientific Director for Etiology, Carl G. Baker, M.D.
Associate Scientific Director for Planning and Analysis, Vacancy.
Associate Scientific Director for Viral Oncology, Frank J. Rauscher, Jr., Ph. D.
Chief, Viral Biology Branch, Albert J. Dalton, Ph. D.
Chief, Viral Carcinogenesis Branch, Robert J. Huebner, M.D.
Chief, Viral Leukemia and Lymphoma Branch, John Moloney, Ph. D.
Associate Scientific Director for Carcinogenesis, Umberto Saffiotti, M.D.
Chief, Biology Branch, Herbert J. Rapp, Sc. D.
Chief, Chemistry Branch, Harry V. Gelboin, Ph. D.
Associate Scientific Director for Demography, Carl G. Baker, M.D., Acting.
Chief, Biometry Branch, William M. Haenszel, M.A.
Chief, Epideminology Branch, Robert W. Miller, M.D., Dr. P.H.
Scientific Director for Chemotherapy, C. Gordon Zubrod, M.D.
Chief, Human Tumor Cell Biology Branch, Seymour M. Perry, M.D.
Chief, Medicine Branch, Paul P. Carbone, M.D.
Associate Scientific Director for Experimental Therapeutics, David P. Rall, M.D., Ph. D.
Chief, Laboratory of Chemical Pharmacology, Vincent T. Oliverio, Ph. D.
Chief, Laboratory of Molecular Pharmacology, Kurt W. Kohn, Ph. D.
Chief, Laboratory of Toxicology, Robert L. Dixon, Ph. D.
Chief, Baltimore Cancer Research Center, Jerome B. Block, M.D.
Chief, Laboratory of Pharmacology (Baltimore), Jerome B. Block, M.D.
Head, Medical Service (Baltimore), Arthur A. Serpick, M.D.
Head, Radiation Therapy (Baltimore), Kirkland C. Brace, M.D.
Head, Neurosurgical Service (Baltimore), Michael D. Walker, M.D.
Chief, Cancer Chemotherapy National Service Center, Saul A. Schepartz, Ph. D.
Associate Chief for Laboratory Research (CCNSC), Abraham Goldin, Ph. D.
Chief, Drug Evaluation Branch, John M. Venditti, Ph. D.

General Laboratories and Clinics

A broad range of research is carried out in both basic laboratories and clinical branches under the general direction of Dr. Nathaniel I. Berlin.

In the Laboratory of Biochemistry, research is directed toward elucidation of neoplastic transformation in molecular terms. To this end, mechanisms of specific biochemical and ultrastructural differentiation, or conversely the loss of specific function, are studied in normal and neoplastic cells. Problems relating to the regulation of protein and nucleic acid biosynthesis are investigated in a spectrum of cultured cell types, in normal liver, bone marrow, and peritoneal cells, in transplantable tumors such as mammary adenocarcinomas and plasmacytomas, and in a wide range of cell-free systems derived from these sources and other sources.

In the Laboratory of Biology, carcinogenesis is studied in the broad biological sense. Attention is given to the manner in which genetic, hormonal, immunological, and viral factors as well as chemical and physical carcinogens lead to the malignant transformation of the cell. Studies are aimed at revealing the nature of this transformation as it occurs under well controlled conditions in tissue culture. Ultrastructure of the cells and the viruses involved are investigated. The role of the thymus in immunology and in viral and chemical carcinogenesis is receiving considerable emphasis. Studies of genetic control of synthesis of abnormal proteins produced by plasma cell tumors and of blood and urinary proteins in mice and subhuman primates are also of primary interest.

In the Macromolecular Biology Section the problems of cell differentiation and growth are approached by studying macromolecular interactions and differential synthesis of biological macromolecules. Studies include differential transcription, nucleic acid homology, translational controls, and the role of cell membranes in regulating cell proliferation.

In the Laboratory of Physiology there are a number of projects which deal primarily with the physiological and biochemical properties of the growing tumor and its impact on the host. Approaches to these problems are made by studies on control of protein synthesis in normal and tumor cells; the mechanisms of synthesis and secretion of hormones on thyroids and thyroid tumor; urinary excretion of purine and pyrimidine congeners and their relation to various types of leukemia; total energy expenditure of the tumor-bearing host as it is derived from both the host and the tumor; characterization and comparison of nucleic acids and nucleo-proteins in bacterial and mammalian tissues, with particular emphasis on elucidating the enzymatic control mechanisms generating in the intact cell; tissue culture studies involving protein synthesis studies during embryonic development; transplantation studies and the immune response; mechanism of repair and recovery of sublethally damaged cells exposed to ionizing radiation; effect of ionizing irradiation on enzyme systems which entails the partial and complete destruction of active centers; antibody formation following multiple irradiation and immunization procedures; radiation damage and recovery of the hemtopoietic system; tissue culture studies to elucidate mechanism of protein synthesis.

The Pathologic Anatomy Branch, provides surgical pathology and autopsy pathology services for all of the clinical programs of the various In-

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stitutes assigned beds in the Clinical Center. The material, therefore, includes a wide variety of neoplastic diseases as well as cardiac, metabolic and infectious diseases in children and adults. The pathologists also conduct independent and collaborative research in many areas of experimental pathology with emphasis on neoplastic disease. The programs include chemical carcinogenesis, viral carcinogenesis and tumor immunology, and they involve laboratory animals and cell cultures as well as field and laboratory studies with human cancer. It offers complete residency training in pathologic anatomy, and research training in the various areas of experimental pathology and carcinogenesis.

In the DERMATOLOGY BRANCH, studies are designed to identify and characterize the biologic behavior patterns of epithelial and lymphoid tissues in normal and pathologic circumstances, using primarily the techniques of biochemistry, electron microscopy, and tissue culture. The chemistry, structure, and function of keratin, melanins and epidermal cell organelles are being investigated, with particular reference to the genodermatoses of man and animals.

In the ENDROCRINOLOGY BRANCH, studies of several aspects of endrocrine physiology are carried out in normal subjects and in patients with endrocrine-responsive tumors. Current research is concentrated in (1) studies of gonadal steroids, secretion and metabolism; (2) studies of protein hormones, with emphasis on gonadotropins and growth hormone; (3) mechanism of steroid action; (4) cytogenetics in patients with developmental abnormalities.

The ENDOCRINE EVALUATION BRANCH sponsors studies on endrocrine factors in relation to breast cancer. This branch also plays an integral part in the Breast Cancer Task Force activities and its program for study and control of breast cancer.

In the IMMUNOLOGY BRANCH, the mechanisms of normal and disordered immune response are under investigation. Physiochemical, immunochemical, tissue culture, isotope incorporation, and *in vivo* turnover techniques are used in research on the structure, biosynthesis, and genetic control of antibodies and of immune cell function. Cell antigens (histocompatability, tumor specific and others), immune cell recognition systems and cellular immunity are parts of fundamental and clinical studies in transplantation (bone marrow) and tumor immunology.

The METABOLISM BRANCH is studying the metabolism of tumors and the effects of tumors upon the metabolism of their hosts. To achieve these objectives, the research program includes studies of the anemia of cancer, porphyrin and bile pigment metabolism, nucleic acid metabolism, calcium metabolism, and the rate of protein synthesis in patients.

Investigations are also directed toward a broad range of immunological problems, especially as they involve immune deficiency states in man associated with a high incidence of malignancies. The studies are concerned with the mechanism of abnormalities of the circulating and cellular immune

responses in patients with such disorders as agammaglobulinemia, the Wiskott-Aldrich syndrome, ataxia telangiectasia, and patients with protein-losing enteropathy and lymphocytopenia. Special attention is given to the study of the factors controlling immunoglobulin metabolism in man and in animal models of immunological deficiency states. In addition, tissue culture techniques are used to determine the role of the macrophage in the immune response.

The Radiation Branch is primarily concerned with the development of new techniques in the treatment of cancer using irradiation alone and in combination with chemotherapy and surgery. Clinical research studies emphasize the malignant lymphomas, chronic lymphocytic leukemia, bone neoplasms, and cancer of the head and neck. Other investigations are directed toward radiation protection and potentiation approaches, including hyperbaric oxygen as an adjunct to radiotherapy. Studies in the radiation physics section are closely integrated with clinical radiotherapy and include computer applications.

Laboratory research is designed to probe for new avenues of treatment with potential clinical application and include radiobiological studies with fast [14 MeV] neutrons and ultra-high dose rates. Considerable attention is devoted to the development of tumor systems in animals which might serve as models for corresponding clinical investigations.

Of major interest to the Surgery Branch is control, through surgery, of pelvic malignancies, tumors of the head and neck area, skin, bone, and soft tissue tumors, and tumors of the urogenital system. Studies of patients with such malignancies are concentrated in three major areas: primary surgical therapy, various aspects of the host response to cancer, and factors associated with the dissemination of cancer.

Etiology

In the Etiology area, a major responsibility of scientists under the direction of Dr. Carl Baker is planning and implementing programed research on cancer causation, patterns of cancer occurrence, and means for cancer prevention.

A program of virus-cancer studies is carried out in the Viral Biology, Viral Leukemia and Lymphoma, and Viral Carcinogenesis Branches. Research activities with DNA and RNA viruses in biological systems range from the subcellular level to that of the intact host, including man. A special program is expanding basic and applied research on the possible viral etiology of leukemia. Institute scientists are collaborating with non-Federal investigators in multidisciplinary studies on animal tumor viruses and in the search for viruses in human cancer.

A special program to provide resource needs of cancer virologists, such as standardized cell lines and new varieties of research animals, is also located in the Viral Carcinogensis Branch.

Chemical hazards in man's environment are of special concern to investigators in the Chemistry and Biology Branches under the Office of the Associate Scientific Director for Carcinogenesis Studies. Emphasis here is placed on the interaction of host factors with multiple environmental factors.

The Epidemiology Branch plans and conducts studies using data from existing sources such as vital and employment records and clinical observations. These investigations seek clues to cancer causation through analysis of interrelationships in the human and domestic animal populations with respect to their total environment and inheritance.

Some of the biostatistical studies carried out by the Biometry Branch are also concerned with the causes of cancer. Others are devoted to evaluating methods for diagnosing and treating cancer. In this connection, more than 100 hospitals in the United States are cooperating in a patient registration and followup program.

Chemotherapy

An intensive program of laboratory research and clinical investigation concerned with the chemical control of cancer is under the direction of Dr. C. Gordon Zubrod.

The Clinical Trials Area emphasizes a multifaceted approach leading to improved management and clinical control of patients with leukemia, lymphoma, and solid tumors with major interests in the acquisition of data from studies of cell kinetics, cytogenetics, biochemical growth characteristics of normal and malignant cells, immune mechanism, etc.

Human Tumor Cell Biology Branch. This Branch has openings for three Clinical Associates yearly. Appointments are for 2 years, but by mutual agreement they may be extended to 3 years. The first year is spent on the wards of the Medicine Branch with responsibility for clinical care of patients undergoing experimental antitumor therapy. The second year consists only of the research work in the laboratories of one of the senior investigators of the Branch.

Research interests include studies of cell kinetics of normal and neoplastic cells, both in leukemia and solid tumors, with emphasis on delineating phases of the cell cycle and characterizing the so-called nonproliferating and proliferating pools. The controls of cellular growth, differentiation, maturation, and the process of malignant transformation in human cells are under intensive investigation with the predominant effort in defining the role of the translational mechanism in neoplasia. Cytogenetic techniques are an integral part of both the kinetic and biochemical studies.

The Medicine Branch has as its objective an indepth approach to the total care of patients with leukemia, lymphoma and solid tumors such as lung cancer and cancer of the breast. The optimal use of new agents, combinations of drugs and maximal supportive care with platelet and leukocyte transfusion and patient protection techniques is investigated in a broad

scale clinical program aimed at improving survival and erradicating the total tumor cell population in these patients. Research interests include the clinical investigation of cellular kinetics, the pharmacology and physiologic disposition of new and established agents, the biochemistry of virus-host interactions and mechanisms of drug action and resistance, the studies of immune mechanisms in cancer including bone marrow transplantation and the immune suppressive effects of drugs, and the improvement in methods for separation, utilization and preservation of platelets and white blood cells from whole blood. The Medicine Branch has two units at the Clinical Center and a joint NCI-Veterans Administration Unit at the District of Columbia Veterans Administration Hospital. In addition a small outpost exists in Kampala, Uganda, designed to investigate Burkitt tumor and other diseases at Makerere University in Kampala, Uganda, Africa.

The Experimental Therapeutics Area studies many facets of the interactions between drugs and living materials. It includes biochemical pharmacology, physiological disposition, drug metabolism, molecular pharmacology and comparative pharmacology. In addition it works closely with the Medicine Branch on clinical research problems. In the Office of the Associate Scientific Director for Experimental Therapeutics, studies on the blood brain and blood cerebrospinal fluid barriers are conducted as well as investigations aimed at improving therapy of brain tumors and meningeal leukemia.

The Laboratory of Chemical Pharmacology is primarily engaged in studies related to the pharmacological disposition of antitumor agents and other drugs in man and animals through the use of established and newly developed analytical-biochemical techniques. Particular emphasis is placed on the study of the influence of simultaneously administered drugs on the distribution, protein binding, metabolism, excretion, and therapeutic activity of the individual agents; the pharmacokinetics of the entry of drugs across membranes into sensitive and resistant tumor cells; structure activity relationship of antitumor agents; new approaches to cancer chemotherapy in general, including studies with macromolecules and the nature of drug receptors; comparative pharmacology; the carcinogenic and other toxicological effects of drugs. Drugs of recent interest have been the folic acid antagonists, nitrosoureas, substituted hydrazines, plant alkaloids and DNA or RNA binding antibiotics, asparaginase and poly I:C. In all areas of interest, both fundamental and mechanistic approaches are utilized.

The Laboratory of Molecular Pharmacology is engaged in physical and biochemical studies on the effects of selected anticancer drugs on DNA. These drug effects are being studied in systems varying in complexity from purified DNA to the intact cell. The objectives are to understand how certain drugs interact with DNA and how the biochemical and physiological consequences of such interactions are expressed. The interactions of drugs with DNA are being examined by physical techniques, and the effects on

DNA-primed RNA synthesis are being investigated in purified enzyme systems, isolated nuclei, and tissue-culture cells. In this regard, the need to understand the state of DNA and the control of its function in nuclei has recently led us to initiate studies on the relations between nucleic acids and proteins in structures such as chromatin. The approach has been to apply methods and data from molecular biology to problems in drug action, and also to use drugs to further our understanding of cell physiology at the molecular level.

The Laboratory of Toxicology functions to investigate and describe the qualitative and quantitative toxicity of potential antineoplastic drugs using animal test systems. Attempts are made to define the predictability, reversibility, and mechanism of drug induced toxicity. Experimental treatment regimens are tested to attain the greatest therapeutic effect at the least cost in serious side effects. The functions of the laboratory are closely integrated with the development of new anticancer agents and ongoing clinical pharmacologic and toxicologic studies.

At the Baltimore Cancer Research Center in the U.S. Public Health Service Hospital, the National Cancer Institute conducts a collaborative program in cancer research and training. A clinical therapeutic program is concerned predominantly with evaluation of chemical agents for the control of neoplastic disease. Additional clinical research programs include radiation therapy, a neurosurgical brain tumor program, studies in septic shock, a program of study, and treatment of infectious complication in cancer and leukemia, a blood component replacement therapy, and clinical pharmacologic investigations of anticancer agents. Separation of human blood cells using continuous flow centrifugation is also being employed. The clinical program is carried out at the USPHS Hospital where there are fully approved residency programs in the major medical specialties. Training is provided to medical students, house officers, and post doctoral fellows. A laboratory program of basic research activities is concerned primarily with pharmacology-oriented investigations with emphasis on lipid and membrane metabolism, drug enzyme interactions, and electron microscopy. There is active investigation of basic tumor immunology as well as immunotherapy of neoplastic disease. These areas are fully integrated with ongoing clinical pharmacologic studies.

The Cancer Chemotherapy National Service Center is engaged in a multidisciplinary approach to the fundamental and developmental aspects of cancer chemotherapy. Through contracts and direct laboratory operations it carries out programs directed toward the development of new and better antitumor agents: The Drug Development Branch is charged with responsibility for production and formulation of drugs for pharmacologic and clinical studies, and the development of new agents from synthetic and natural sources; the Drug Evaluation Branch is concerned with the evaluation of such agents in experimental test systems, development of new methods for drug evaluation, and detailed studies of optimal drug dosages

and regimens; within the Office of the Chief, research programs are concerned with establishment of new therapeutic principles, methodologic studies on the development of new screening systems, studies of drug resistance and mechanism of action, and animal genetics and disease control.

Other Training Programs

In addition to the research areas described, there are opportunities for those interested in data processing and information flow in this national drug development program.

In the Program Analysis Branch there are opportunities for those interested in operations research, systems analysis, and computer programing as related to the data retrieval analysis of this national effort. A recent project included statistical analyses (including life-table preparation) of long-term survivors having acute leukemia and Hodgkin's disease.

The Cancer Therapy Evaluation Branch coordinates the inflow of information on the various clinical trials performed with the many investigational new drugs sponsored by the Chemotherapy area of the National Cancer Institute. It handles the liaison with the Food and Drug Administration as well as coordinating the details of drug distribution and protocol handling. It serves as a liaison with the various cancer chemotherapy cooperative groups and task forces. Internally, the branch handles the inflow of both preclinical and clinical information into the various decision networks of the new chemotherapy linear array system.

National Eye Institute

Carl Kupfer, M.D., Director

General. The National Eye Institute conducts, fosters and supports research and training on the cause, natural history, prevention, diagnosis, and treatment of disorders of the eye and visual system and in related fields.

CORD deferments for approved clinical training beyond a year of internship are available for some positions.

Intramural Research Program

Carl Kupfer, M.D., Director

The Ophthalmology Branch has clinical programs with the following disease groups: Uveitis, glaucoma, retinal degenerations, vascular retinopathies, tumors of the eye, and cataract. The Office of the Chief also conducts research on cell population dynamics studies on eye tissue; effect of cytotoxic agents on the lens epithelium.

There are five laboratory sections: (1) Physiology (Head, Dr. P. Gouras)—physiological studies of visual neurons and their relationship to psychophysics of vision; (2) Metabolism (Head, Dr. P. O'Brien)—studies on amino sugar metabolism and glycoprotein and polysaccharide synthesis in the retina; (3) Pharmacology (Head, Dr. F. Macri)—studies on aqueous dynamics and intraocular pressure; on pressure and perfusate flow rate in intraocular vessels; (4) Chemistry (Head, Dr. M. Lewis)—physicochemical studies on collagen of the cornea, sclera, and vitreous body; (5) Experimental Embryology (Head, Dr. A. Coulombre)—Morphogenesis of the vertebrate visual system.

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National Heart and Lung Institute

Donald S. Fredrickson, M.D., Director of Intramural Research

A. Associate Program in Medicine and Basic Science

The National Heart and Lung Institute currently appoints three Research Associates and six Clinical Associates for a 2-year period beginning each July 1. Several Staff Associates are also usually appointed in one or more of the Institute's laboratories. For those who are interested in lengthening their period of research experience, these appointments may, by mutual agreement, usually be extended for a third year.

Candidates may apply for one or more types of Associate positions. In selection of Associates preference is given to candidates who intend to devote a significant portion of their career to research. Because of the diversity of the Heart and Lung Institute program, special interest in cardiovascular disease is not an essential requirement.

Research and Clinical Associates

Candidates for Research and Clinical Associate positions have only one interview in the Heart and Lung Institute. Each Associate is free to choose his own area of research assignment. After his appointment and prior to his entering on duty, he will make a separate visit, at Institute expense, to select the laboratory in which he will work. The choice is based on the background and interests of the Associate and is contingent only on the ability of the particular laboratory to furnish proper supervision and facilities. (On the basis of past experience, it would appear virtually certain that each Associate will be able to work with the group of his choice.) The level of research responsibility and freedom will depend upon his training and experience as well as his desires.

Research Associates. These appointments are designed to give physicians an opportunity to improve their background for a career in basic medical research. Usually physicians enter the appointment after completing internship and 1 year residency, but there are no specific requirements for postgraduate training after the M.D. degree.

Each Research Associate will devote his time to research in the laboratory under the immediate supervision of a preceptor in an area of his selection. Each will select appropriate courses in the basic, medical and allied sciences, and seminar and journal club exercises common to the

program arranged for Research Associates of all the Institutes. No clinical assignments are involved, but the Associates are welcome to attend any of the clinical teaching exercises.

Clinical Associates. These appointments are designed to give physicians training in both clinical and basic research. Candidates must have completed a minimum of 1 year of internship plus 1 year of residency in internal medicine by the starting date of their appointment.

Clinical Associates will be responsible, under the guidance of investigators on the Heart and Lung Institute staff, for the medical care of patients during 10 of the first 14 months of their service. During this time they will rotate through the four medical services that serve the medically oriented Branches of the Heart and Lung Institute. These services occupy 85 beds and include: (1) Cardiology; (2) Endocrinology; (3) Experimental Therapeutics; and (4) Molecular Disease.

The clinical period is one of intensive training under direction of the Clinical Director and staff. It offers exposure to case material of an extraordinary range and to highly sophisticated approaches to investigation of disease.

The Clinical Associate devotes both his time off the wards and a full 14 months of his 2-year assignment to laboratory research under direction of a preceptor *in any one of the Heart and Lung Institute laboratories, either clinical or nonclinical.* No clinical responsibilities are required during the optional third year. The Associate may also participate in seminars and instruction available to the Research Associate.

Staff Associates. Laboratories within the Heart and Lung Institute sometimes have openings for Staff Associates appointed from the Matching Program. When such appointments are available they are listed in the Program Area Selection Check List for the Institute. Selections for those positions are made by the Chief of the Laboratory.

Formal Instruction

The major form of didactic postgraduate instruction is through the evening courses offered by the Graduate Program of the Foundation for Advanced Education in the Sciences, Inc. Research, Clinical, and Staff Associates are expected to take advantage of this academic work.

B. Associate Program in Surgery

The Surgery Branch of the National Heart and Lung Institute appoints approximately five Associates in Surgery for a 2-year period beginning each July 1. The program is primarily designed for young surgeons with primary interests in cardiovascular surgery and cardiovascular physiology. In making appointments, preference will be given to candidates contemplating a career in a research or academic atmosphere. Candidates must have completed an internship and at least 1 year of surgical residence by the starting date of their appointment.

Approximately 1 year is devoted to an intensive clinical experience involving the management of patients undergoing operations for congenital and acquired heart disease. During this period the majority of Associates are also trained in the techniques of cardiac catheterization and angiography and in the interpretation of clinical physiologic data. A period of approximately 1 year is also devoted to research in the experimental surgery laboratory and in clinical investigations related to operative procedures. This work, carried out in association with staff members, will be in the general field of cardiovascular physiology as applied to the treatment of surgical patients.

Laboratories and Sections

The laboratories and sections of the National Heart and Lung Institute, all of which are open to Clinical and Research Associates for their research work, are listed below with the names of their chiefs and a brief summary statement indicating the breadth of activities. Candidates desiring further information may obtain a current bibliography summarizing the activities of the current staff by writing to Dr. Donald S. Fredrickson, Director of Intramural Research, National Heart and Lung Institute, Bethesda, Md. 20014.

Laboratory of Biochemical Genetics (Chief, Dr. Marshall Nirenberg). Molecular mechanisms for the storage and retrieval of information at the level of the gene are under study. For aspects of these studies involving particularly the flow of information from cell to cell, the neuron is used as a model system.

Laboratory of Biochemistry (Chief, Dr. Earl R. Stadtman).

Section on Enzymes (Head, Dr. Earl R. Stadtman). Studies of diverse enzyme systems that offer unique opportunities to elucidate a number of basic biochemical phenomena, namely, those concerned with vitamin-coenzyme function, the cellular regulation of metabolism, the energy-dependent transport of metabolites across membrane barriers, and mechanisms of enzyme action.

Section on Cellular Physiology (Head, Dr. Wayne Kielley). This section conducts studies of the structural basis for the biochemical properties of protein molecules and their integrated function in cellular structures.

Section on Cellular Biochemistry and Ultrastructure (Head, Dr. Edward D. Korn). It is the purpose of this section to study structural and functional relationships at the cellular level. Biochemical and ultrastructural methods are used in tandem in order to establish the morphological basis for the biochemical event and the biochemical function of the structural element.

Section on Cellular Differentiation (Head, Dr. Bennett M. Shapiro). This section is concerned with investigations of the biochemical aspects of cellular division and differentiation.

Laboratory of Chemical Pharmacology (Chief, Dr. Bernard B. Brodie).

Section on Clinical Pharmacology (Head, Dr. Bernard B. Brodie). Explores biochemical and physiological mechanisms of drug action including the functions of the autonomic nervous system, the role of adrenocortical, thyroid and other hormone systems in regulating the autonomic and central nervous systems and the processes that control the tissue levels of biogenic amines, acetylcholine, and c–AMP. The Section also explores mechanisms of idiosyncratic effects of drugs.

Section on Enzyme Drug Interaction (Head, Dr. James R. Gillette). Studies various aspects of drug disposition including the mechanism of drug-metabolizing enzymes in liver microsomes, the factors which alter the activity of these enzymes, and the relationship between the metabolism and toxicity of drugs.

Section on Organic Chemistry (Head, Dr. Elwood O. Titus). Studies isolation and characterization of those cellular components, usually membrane proteins, which serve as the targets for drugs and hormones affecting the cardiovascular system and carries out physical chemical studies of the mechanisms by which drugs interact with these components.

Section on Physiology (Head, Dr. Harriet M. Maling). Studies the cardiovascular, behavioral, and other physiological responses to drugs and correlates these responses with biochemical effects.

Laboratory of Kidney and Electrolyte Metabolism (Chief, Dr. Jack Orloff).

Section on Electrolyte Transport.

Section on Experimental Cardiovascular Diseases.

Section on Renal Mechanisms.

This laboratory conducts research on the mechanism and regulation of a variety of transport processes in systems including the intact kidney, isolated segments of renal tubules, toad bladder, erythrocyte, and muscle.

Laboratory of Technical Development (Chief, Dr. Robert L. Bowman). Conducts research into instrumentation and methodology applicable in heart and biomedical research. The scope of the program includes practical clinical devices for artificial support of the circulatory and respiratory systems through advances in ultramicrochemical analytical techniques.

Cardiology Branch (Chief, Dr. Stephen E. Epstein).

Section on Cardiovascular Diagnosis (Head, Dr. David L. Glancy). Investigations are oriented toward the diagnosis of acquired and congenital heart disease, the evaluation of operative and nonoperative forms of treatment, and the elucidation of mechanisms responsible for the hemodynamic changes produced by heart failure.

Section on Clinical Physiology (Head, Dr. Stephen E. Epstein). Research objectives are aimed toward an understanding of the physiologic and biochemical mechanisms responsible for the control of the heart and circulation.

Section on Clinical Biophysics (Head, Dr. Donald L. Fry). The program is directed toward study of basic vascular rheology and hydrodynamics with particular reference to how these relate to atherosclerosis.

Section of Pathology (Head, Dr. William C. Roberts). This section is concerned with the study of morphologic aspects of cardiovascular disease and correlating them with functional derangements. Morphologic analyses include electron microscopy.

Section on Cardiovascular Pharmacology (Head, Dr. Theodore Cooper). Current work is concerned with a comprehensive study of the terminal nervous innervation of the heart and how it is altered following denervation or transplantation procedures. The methods used in these studies are electrophysiology, pharmacology, and electron microscopy.

Endocrinology Branch (Chief, Dr. Frederic C. Bartter).

Section on Steroid Metabolism and Hypertension (Head, Dr. Frederic C. Bartter).

Section on Mineral Metabolism (Head, Dr. Charles Y. C. Pak).

The principal research of this Laboratory is involved with the functions of the adrenal glands, parathyroid glands, the pituitary gland, and the kidneys. Both basic laboratory work (concerned with underlying biochemical, physicochemical or physiological mechanisms) and clinical research of endocrine disorders are carried out.

Experimental Therapeutics Branch (Chief, Dr. Albert Sjoerdsma).

Section on Experimental Medicine (Head, Dr. Albert Sjoerdsma). Offers a spectrum of research opportunity ranging from basic biochemistry and pharmacology to the study of chemical factors in disease and clinical response to drugs. Current studies encompass disorders of amine metabolism (catecholamines, serotonin), biochemistry of sleep and collagen disease. Studies on essential hypertension are conducted both in man and in experimental models in the rat.

Section on Biochemical Pharmacology (Head, Dr. Walter M. Lovenberg). Conducts a broad research program in the biochemistry and pharmacology of aromatic amines, the physical and chemical properties of certain metalloproteins, specifically, adrenodoxin, clostridial ferredoxin and rubredoxin, and the electron transport properties of artificial nonheme iron protein.

Section on Peptide Biochemistry (Head, Dr. John J. Pisano). Studies concerned with the identification, biosynthesis, assay, and met-

abolic significance of biologically active peptides, related precursors and enzymes. The scope of activities includes the development of necessary new analytical procedures and the study of normal and pathological conditions in man.

Section on Neuroendocrinology (Head, Dr. Robert I. Henkin). Devoted to the study of the interrelationships between the nervous and the endocrine systems in three interrelated areas: (1) the effects of steroid hormones on nervous system activity as well as steroid localization and metabolism in the nervous system; (2) mechanisms of function of gustation and olfaction as represented in various disease states; and (3) the effects of trace metals in neuroendocrine metabolism, in various altered metabolic states and as indicators and treatment in various gustatory and olfactory abnormalities.

Molecular Disease Branch (Chief, Dr. Donald S. Fredrickson).

Section on Chemistry (Head, Dr. Henry M. Fales). Concerned with research into the structure of organic compounds of biological interest and with the development of methods and techniques related to such studies.

Section on Human Biochemistry (Head, Dr. W. French Anderson). Concerned with investigations into the mechanism and regulation of mammalian protein synthesis, specifically relating to hemoglobin and diseases involving the regulation of hemoglobin synthesis.

Section on Molecular Diseases (Head, Dr. Donald S. Fredrickson).

Section on Lipoproteins (Head, Dr. Robert I. Levy).

Section on Molecular Structure (Head, Dr. Antonio M. Gotto).

The work of the three sections listed above is primarily concerned with an integrated study of fat transport in plasma, including the structure, metabolism, and functions of lipoproteins, and genetically determined disorders relating to lipid transport and metabolism and to atherosclerosis.

Section on Metabolism (Head, Dr. Martha Vaughan). Concerned with the mechanisms underlying hormonal regulation of metabolism, particularly the control of lipolysis in adipose tissue and the role of cyclic AMP in this and other tissues.

Surgery Branch (Chief, Dr. Andrew G. Morrow).

National Institute of Allergy and Infectious Diseases

John R. Seal, M.D., Scientific Director

John E. Tobie, Ph. D., Assistant Scientific Director for Laboratory and Clinical Research

Clinical Associates

The Laboratory of Clinical Investigation (Sheldon M. Wolff, M.D., Clinical Director)

The National Institute of Allergy and Infectious Diseases appoints six to eight Clinical Associates. Appointments are made for 3 years. Ward medical care duties occur during the first year, and no assigned clinical responsibilities are made during the second or third year except as dictated by the needs of the Clinical Associates' research.

There are 52 research beds. Clinical Associates consult on clinical infectious disease problems in other Institutes. Each Clinical Associate selects his own area of investigative interest under the general preceptorship of the Clinical Director and the senior members of the staff of the Laboratory of Clinical Investigation. Emphasis is placed on the conduct of laboratory and clinical research designed to provide the basic training necessary for a career in clinical investigation.

Opportunities exist for research in a wide variety of areas of infectious and immunological disease. Examples of studies now in progress are:

- Elucidation and evaluation of immunologic and nonimmunologic events induced in humans and animals by viral infection or vaccination.
- Antifungal chemotherapy, analysis of antigenic constituents of fungi, and development of diagnostic skin and serologic tests for mycoses.
- Pathogenesis of both experimental and clinical fevers.
- The role of the granulocyte in resistance and response to infection.
- The mechanism of immune damage and the role of complement in immunological reactions.
- The influence of drugs and hormones on hepatic hemoproteins and drug metabolizing capacity.

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- Biochemical and morphologic properties of lysosomes and the lysosomal enzymes of human leucocytes to determine their role in the pathogenesis of certain inflammatory diseases.
- The biochemical response in lymphoid cells following antigenic stimulation in normal and immunologically impaired subjects.
- The pathogenic mechanisms of the aspirin sensitivity-asthma syndromes.
- The structure and function of immunoglobulins of human and lower animal origin.
- The application of electron microscopy, autoradiographic, and cytochemical techniques to studies of cellular interactions in immunologic information processing both in humoral and cellular events.
- The role of the reticuloendothelial system in host defenses against clinical and experimental infections.
- Research in both the clinical and laboratory aspects of parasitic diseases.

Further information can be obtained if inquiries with specific questions are addressed to Dr. Sheldon M. Wolff.

Other Associates

A variable number of other associates are selected each year for work in the laboratories listed below. CORD deferments are, for the most part, related to those appointments where there is advantage to the laboratory in the additional training. Other associate appointments begin upon completion of internship. Appointees may change their laboratory and preceptor either before or on arrival for duty by consultation with the Scientific Director.

The Laboratory of Viral Diseases (Wallace P. Rowe, M.D., Chief) conducts research on the basic biology and ecology of chronic and persistent virus infections, with particular emphasis on oncogenic viruses, and on host antiviral defense mechanisms.

Studies of tumor viruses are concentrated on murine leukemia viruses, SV40, adenovirus–SV40 hybrid viruses, and Marek's disease of chickens. These studies include investigations of the interactions between defective and competent viruses, etiology of naturally occurring animal tumors, serologic characterization of viral products, and genetics of the viruses.

The mechanism of action of interferon and inducers of interferon is studied by biological and biochemical approaches. The laboratory will be participating in clinical evaluation of interferon inducers in a variety of diseases.

Associates coming in 1971 will participate in the interferon program, and those in 1972 will be assigned to the tumor virus area.

The Laboratory of Biology of Viruses (Norman P. Salzman, Ph. D., Chief) conducts studies relating to the mode of replication of animal and human viruses. Investigations are conducted to define the molecular basis

for the pathogenic effects of viruses on cellular functions. Enzymes induced following virus infection and the products of these enzymes are investigated. These studies are carried out with both lytic and oncogenic viruses. Fundamental biochemical and biophysical studies are also carried out with uninfected cells. The mechanisms by which normal cells are transformed to an oncogenic state are also studied.

Parallel studies to those on viral synthesis seek to define the physical and chemical makeup of the purified virus itself, utilizing electron microscopy, ultracentrifugation, and nucleic acid and protein analysis.

Other programs investigate the isolation and characterization of mutated viruses. Studies are conducted on the relationship between alterations in the viral genome and biochemical alterations in the infectious cycle.

The program is designed to give Research and Staff Associates a full understanding of modern trends in molecular biology and to enable them to apply biochemical and biophysical techniques in dealing with fundamental problems in the area of animal virology and cell biology.

The Laboratory of Infectious Diseases (Robert M. Chanock, M.D., Chief) is concerned with the basic behavior of viral and mycoplasmal pathogens which play in important role in acute infectious diseases of man. The importance, disease manifestations and ecologic properties of various respiratory tract pathogens are defined during the study of individuals with naturally acquired disease. Supplementary information is obtained from detailed investigation of experimentally infected volunteers in an attempt to define the pathogenesis of disease and the factors involved in the hosts' resistance to both infection and illness. The techniques of microbial genetics are employed to study the nature of virulence and to select attenuated mutants which are then evaluated for their usefulness in vaccination against natural disease.

Biophysical techniques are used to define the subparticulate structure of viruses and to search for certain fastidious agents, such as coronaviruses and hepatitis viruses, which cannot be detected in standard tissue culture systems. Appointees can expect to receive training in basic biophysical and biological characterization of viruses and mycoplasmas, microbial genetics, immunologic methods used in the study of respiratory tract disease and epidemiologic techniques employed in defining the ecology of agents which cause acute infectious diseases.

The Laboratory of Immunology (Dr. Baruj Benacerraf, Chief) is engaged in the study of basic immunological phenomena as well as in the application of the knowledge gained to the solution of current medical immunological problems.

Modern techniques of biochemistry, immunochemistry, immunobiology, genetics and molecular biology are available and used for these purposes.

The basic immunological phenomena currently investigated are:

1. Studies on the nature of antigenicity and on the specificity and diversity of the immune response at the humoral and cellular levels with synthetic polypeptide antigens of defined structure and sequence and with hapten conjugates of these compounds.

2. Studies of the genetic factors which control the recognition of immunogenicity and the development of the immune response. An attempt is made to identify by transfer experiments the cell type which expresses phenotypically the genetic control of the immune response observed in mice and guinea pigs against certain synthetic antigens.

3. Studies of the genetic control of the structure of immunoglobulin chains through the investigation of their allotypic markers and their genetic recombination.

4. Studies on the structure of rabbits and mice immunoglobulin chains in relation to their allotypic markers.

5. Studies on the mechanism of tolerance with protein and polysaccharide antigens both *in vivo* and *in vitro* and investigations of the comparative specificities of tolerance and immunity to the same antigen.

6. Studies on the factors which control the immune response at the cellular level *in vivo* and *in vitro;* the role of antigen and specific antibody. Studies of the factors which control the proliferative response of sensitized cells to antigen and the mechanism of cell selection by antigen.

7. Studies on the properties of the antigen receptors (cell bound antibodies) of specific immunocompetent cells.

8. Studies on the nature and significance of cell to cell interactions in the immune response such as macrophage-lymphocyte interaction and interaction of thymus derived cells and bone marrow cells.

9. Studies on the mechanism of delayed hypersensitivity. Genetics of hypersensitivity phenomena.

10. Preparation and characterization of soluble guinea pig and human transplantation antigens. Studies in guinea pigs of the metabolism of such transplantation antigens in an attempt to develop specific tolerance to homograft without or with a minimum of immunosuppressive therapy.

The Laboratory of Microbial Immunity (John E. Tobie, Ph. D., Chief) is concerned with fundamental studies on host responses to microorganisms and on transplantation immunity. A germfree facility within the Laboratory is available which provides germfree species as significant tools for investigating the mechanisms of the immune response. Basic research is conducted on the induction and control of immunoglobulin synthesis. Immune responses of hosts to living microbial agents or antigenic fractions of microorganisms are evaluated by a variety of methods including the fluorescent antibody technique and immunoglobulins are quantitated by gel diffusion methods. Autoimmune phenomena, such as those observed in allergic thyroiditis, are studied in laboratory animal models and factors which

regulate development and severity of the disease are elucidated. The induction of antibody synthesis and the development of immunological tolerance to pneumococcal polysaccharides is investigated at the cellular level. In transplantation research the suppressive effects of antilymphocyte serum on the homograft reaction and the development of other methods for prevention of homograft rejection are intensively studied. The nature of the graft-*versus*-host reaction mediated by different populations of lymphoid cells is investigated. Methods of fractionating lymphoid cells are explored so that cells mediating various immunological reactions can be concentrated and purified.

The Laboratory of Parasitic Diseases (Franklin A. Neva, M.D., Chief). Intramural Research activities in the area of parasitic diseases have been reorganized. They are under the overall direction of Franklin A. Neva, M.D., Chief. The general areas of interest which have characterized previously existing laboratories will be continued. Thus, research on malaria is pursued at the laboratories in Bethesda as well as at a special facility in Chamblee and Atlanta, Ga. Fundamental and applied studies on a variety of other parasitic disease entities are carried out in Bethesda.

The research program on malaria covers many different aspects of the subject and includes work on modes of action of chemotherapeutic agents, problems of drug resistance, biology of human and simian malarial parasites, immune mechanisms, immunodiagnostic methodology, the arthropod vectors of malaria, and pathophysiology of malaria. The laboratory facilities at Chamblee, Ga., are uniquely equipped for work with malaria in primates and an insectary for work with malaria vectors. Closely related to the unit in Chamblee is a facility in adjoining Atlanta for work with malaria in human volunteers. The combined facilities offer almost unparalleled opportunities for work on malaria in man or in animal models and on all stages of the life cycle of the parasite.

Research on parasitic diseases at Bethesda encompasses a variety of entities in addition to work on malaria. The facility at Bethesda has a long history of interest and continued study in toxoplasmosis, trypanosomiasis and leishmaniasis, schistosomiasis, amebiasis, and filariasis. One approach that is used for research in these subjects is to apply basic scientific disciplines such as biochemistry or immunology to the study of different parasites. For example, one group with broad interest in comparative physiology of parasites is working on energy transfer in vertebrate and invertebrate cells. Another group is studying nucleic acid metabolism and using the techniques of nucleic acid homology to compare different species and strains of amoebae. Ultrastructure of parasites and relationship of their structures to function represents still another area of study. A second research approach that is represented in the Laboratory is the study of some aspect of specific parasitic disease entities. Examples of such current work include investiga-

tions in the pathogenesis of schistosomiasis, filariasis, and Chagas' disease, with particular emphasis upon immunity and hypersensitivity as factors in the host-parasite relationship.

Since Dr. Neva is associated with the Laboratory of Clinical Investigation (Section on Parasitic Diseases), opportunity exists to develop a closer relationship between clinical and laboratory studies on parasitic disease problems.

The Laboratory of Microbiology (Roger M. Cole, Ph. D., M.D., Chief) is engaged in basic studies of bacteria, mycoplasma, and fungi. Streptococci, staphylococci, and a *Hydrogenomonas* are the principal bacterial subjects of current investigation. Areas of study include streptoccocal genetics and bacteriophage; the nature, identification, induction, and reversion of bacterial L-phase growth and its role in pathogenicity and disease; the role of iron in nonspecific immunity and in bacterial metabolism; bacterial cell walls and autolytic enzymes; isolation and function of membranous organelles from cocci; the electron transport system of hydrogen utilizing autotrophs; composition, synthesis, and modification of naturally-occurring and synthetic antimicrobial agents; the nature and isolation of some *Mycoplasma* antigens; ultrastructure of bacteria and other microorganisms; and pathogenesis of lesions inducted by streptococcal fractions and products.

The Mycoplasma Section is investigating, by cultural, metabolic, and serologic methods, taxonomic relationships among the mycoplasma. In addition, the pathogenicity, and role in disease, of these microorganisms is under study.

In medical mycology, utilizing *Histoplasma, Coccidioides, Candida, Cryptococcus, Nannizzia,* and *Blastomyces* there are current studies on physiology and nutrition; effects of experimental chemotherapeutic agents; ecology and interrelationships of soil microflora; genetics of pathogenic fungi; and immunology and immunochemistry of yeast polysaccharides.

The Middle America Research Unit (Karl M. Johnson, M.D., Director) is located in the Panama Canal Zone and is a joint enterprise of the PHS and the U.S. Army. This well-equipped laboratory is engaged in the study of Bolivian hemorrhagic fever, a viral disease with high mortality. Areas emphasized include epidemiology and field ecology in Bolivia, comparative virological investigation of the causative agent and its immunologic relatives, and the biological behavior of the virus in its natural rodent reservoir *Calomys callosus*. Epidemiological work on several arthropod-transmitted virus diseases such as Venezuelan equine encephalitis and St. Louis encephalitis continues. Field studies in several countries provide materials for laboratory-based efforts to develop new techniques for understanding the complex life-cycles of these infections in the tropics. Recent work documented the importance of geographic variation in virus strains; immunological studies are in progress to assess the importance of this finding both in terms

of evolutional biological theory and practical public health application. The ecology of vesicular stomatitis virus infection is being investigated. Since the mode of virus transmission is unknown, work includes field observations, experimental studies of certain arthropods, and virological and immunological investigations of virus behavior in tropical vertebrates.

Through liason with the U.S. Army component, opportunities are available for laboratory and field study of certain parasitic diseases, particularly toxoplasmosis, leishmaniasis, and American trypanosomiasis.

The Rocky Mountain Laboratory (Herbert G. Stoenner, D.V.M., Director), located at Hamilton, Mont., is internationally recognized for research on rickettsial and tick-borne diseases. In medical entomology and acarology, principal projects include biology and systematics of ticks and mites, ecology of selected tick- and mosquito-borne viruses, and general and subcellular relationships between arthropod-borne microbiota and their vectors as studied by various approaches, including arthropod tissue culture and electron microscopy.

Various aspects, particularly immunology and microbiology, of selected infectious diseases are under investigation. Scrapie and progressive pneumonia of sheep, and Aleutian disease and encephalopathy of mink are studied as models of chronic degenerative diseases of man. Limited studies are made on rabies, tularemia, and the PLT group of organisms. More basic inquiries are made into fundamental mechanisms in delayed hypersensitivity and antibody production according to immunoglobulin class.

The fractionation of microbial agents, such as *Mycobacteria, Bordetella,* and Gram-negative organisms, by special biophysical and biochemical methods and the role of these subcellular fractions in immunity, hypersensitivity and other host responses are subjects of major investigations.

Opportunities for training associated with these research projects are provided in comparative pathology, electron microscopy, virology, immunology, immunochemistry, and a wide variety of specialized biophysical and biochemical methodolgy.

Other Opportunities

The Pakistan-SEATO Cholera Research Laboratory, Dacca, East Pakistan (PSCRL) (Dr. Robert A. Phillips, M.D., Director) is managed by the Scientific Director. This offers opportunity for training and research in gastrointestinal physiology and immunology as they relate to cholera and other endemic diseases of the area. CORD deferments will be utilized to provide necessary training before assignment. Those interested should contact the Scientific Director for further information.

Additional information on any laboratory may be obtained by writing to Dr. John R. Seal, Scientific Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. 20014. Those interested in either the Middle America Research Unit or the Rocky Mountain Laboratory will be interviewed in Bethesda but should at least correspond with the Laboratory Chief in terms of opportunities and mutuality of interests.

National Institute of Arthritis and Metabolic Diseases

J. E. Rall, M.D., Ph. D., Director of Intramural Research

Robert S. Gordon, Jr., M.D., Clinical Director

Clinical Associates

The NIAMD appoints approximately ten Clinical Associates each year. The assignments are for 2 years, and ordinarily are not extended. A limited number of opportunities exist for outstanding Associates to extend their stay for an additional year, or to be considered for appointment to other positions.

Each Clinical Associate is attached for his 2-year duty period to one of the clinical branches or sections, within which he carries out both clinical work and laboratory studies. He is, in effect, an apprentice clinical investigator, working both on the wards and in the laboratory under the guidance of an experienced preceptor. The Associate is encouraged to choose his own problem for independent investigation, subject to the limitation that the facilities required for its successful pursuit, and the technical advice and supervision necessary, must be available to the branch or section in which he is to be working. In addition, he provides professional care for the research patients admitted to the service of his branch chief, and assists in the work of that branch in the outpatient department. There is considerable variation among the branches of NIAMD with respect to the proportion of the Associate's time required for patient care activities.

Since appointments are for 2 years, vacancies do not necessarily occur within each program area each year. The chiefs of branches or sections having openings for new Clinical Associates, and the Clinical Director, screen applications and select candidates for personal interviews. After interviews are completed and the results of matching are announced, each successful candidate is asked to confirm his acceptance of the position with which he was matched. It is not possible, after this, to change the Associate's assignment within NIAMD.

The list below identifies all of the clinical research branches within NIAMD, and their sections, by title and by the name of the chief. The Program Area Selection Check List indicates those having vacancies to be filled at this time. Prospective applicants who are not familiar with the

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qualifications and research accomplishments of the branch and section chiefs, or with the details of their current investigative and clinical programs, are encouraged to write Dr. Robert S. Gordon, Clinical Director, NIAMD, Building 10, Room 9N–222, Bethesda, Md. 20014. Supplementary information sheets on each branch, together with selected bibliographic citations, are available on request.

Clinical Associate in Experimental Pathology

In addition to Clinical Associates who take care of patients on wards in the Clinical Center, the Laboratory of Experimental Pathology has clinical responsibility for surgical and autopsy material. This Laboratory appoints approximately two Clinical Associates in Experimental Pathology each year. Further information can be obtained from Dr. Gert L. Laqueur, Chief of the Laboratory of Experimental Pathology.

Research Associates

The National Institute of Arthritis and Metabolic Diseases has four positions available each year for Research Associates. These 2-year appointment, usually beginning on July 1, are designed to give highly qualified physicians an opportunity to improve their background for careers in basic medical research. During his stay here, each Research Associate will devote the larger part of his time to participation in laboratory research under the immediate supervision of a preceptor. The chosen candidates are free to choose a preceptor (upon mutual agreement) in any area in the Institute, either clinical or basic research. Should he elect a clinical area, he would not participate in clinical care of patients. The Research Associate, approximately 1 year prior to beginning, will visit NIAMD to select the laboratory and preceptor with whom he wishes to work. Candidates desiring further information about the laboratories, staff and bibliography of NIAMD may obtain this by writing to Dr. J. E. Rall, Director of Intramural Research, NIAMD, National Institutes of Health, Bethesda, Md. 20014.

Clinical Research Branches

Arthritis and Rheumatism Branch—Dr. John L. Decker
  Section on Connective Tissue Disease—Drs. John L. Decker, Norman L. Talal, Henry Metzger, and Peter Goldman.
Clinical Endocrinology Branch—Dr. Jacob Robbins
  Section on Diabetes and Intermediary Metabolism—Drs. Jesse Roth, Phillip Gorden, and Robert Perlman.
  Section of Endocrine Biochemistry—Drs. Jacob Robbins, Jan Wolff, Saul Rosen, Hans Cahnmann, Harold Edelhoch, and Charles Lewallen
Clinical Hematology Branch—Dr. N. Raphael Shulman
Digestive and Hereditary Diseases Branch—Dr. Leonard Laster
Metabolic Diseases Branch—Dr. Robert S. Gordon, Jr.

Section on Mineral Metabolism—Dr. Gerald D. Aurbach
Section on Physiology and Clinical Nutrition—Dr. Robert S. Gordon, Jr.
Section on Diseases of the American Indian—Dr. Robert S. Gordon, Jr. (Acting)
Pediatric Metabolism Branch—Dr. Paul A. diSant'Agnese

Basic Research Laboratories

Mathematic Research Branch—Dr. John Z. Hearon
Laboratory of Nutrition and Endocrinology—Dr. Herbert Sober
Section on Nutrition Biochemistry—Dr. John G. Bieri
Section on Endocrinology—Dr. Robert O. Scow
Section on Vitamin Metabolism—Dr. Bernard Kaufman
Laboratory of Biochemistry and Metabolism—Dr. Gilbert Ashwell
Section on Enzymes and Cellular Biochemistry—Dr. William Jakoby
Section on Intermediary Metabolism—Dr. Yale J. Topper
Laboratory of Experimental Pathology—Dr. Gert L. Laqueur
Section on Histochemistry—Dr. George G. Glenner
Section on Chemical Pathology—Dr. Vincent Marchesi
Section on Biophysical Histology—Dr. Ned Feder
Section on Rheumatic Diseases—Dr. Leon Sokoloff
Laboratory of Biochemical Pharmacology—Dr. Herbert Tabor
Section on Pharmacology—Dr. Herbert Tabor
Section on Biochemical Regulation—Vacancy
Section on Biochemistry—Dr. Victor Ginsburg
Section on Biochemistry of Amino Acids—Dr. Simon Black
Laboratory of Chemistry—Dr. Bernhard Witkop
Section on Carbohydrates—Dr. Hewitt G. Fletcher, Jr.
Section on Medicinal Chemistry—Dr. Everette L. May
Section on Steroids—Dr. Yoshio Sato
Section on Biochemical Mechanisms—Dr. Louis A. Cohen
Section on Metabolites—Dr. Bernhard Witkop
Section on Microanalytical Services and Instrumentation—Dr. William Alford
Laboratory of Physical Biology—Dr. John Buck
Section on Comparative Physiology—Dr. John Buck
Section on Molecular Biophysics—Dr. Edwin D. Becker
Section on Electrochemistry and Colloid Physics—Dr. Karl Sollner
Section on Cellular Physics—Dr. Richard J. Podolsky
Section on Physiology—Dr. Paul D. Altland
Laboratory of Molecular Biology—Dr. Gary Felsenfeld
Section on Metabolic Enzymes—Dr. Martin Gellert
Section on Chemical Genetics—Dr. Harvey A. Itano
Section on Physical Chemistry—Dr. Gary Felsenfeld
Section on Molecular Structure—Dr. David R. Davies

Section on Microbial Genetics—Dr. Robert Martin
Section on Organic Chemistry—Dr. H. Todd Miles
Laboratory of Chemical Biology—Dr. Christian B. Anfinsen
Section on Biosynthesis and Control—Dr. Robert Goldberger
Section on Protein Chemistry—Dr. Christian B. Anfinsen
Laboratory of Biophysical Chemistry—Dr. Koloman Laki
Section on Bioenergetics—Dr. William J. Bowen
Section on Macromolecules—Dr. Harry A. Saroff
Section on Physical Biochemistry—Dr. Koloman Laki

National Institute of Child Health and Human Development

Gerald D. LaVeck, M.D., Director
Charles U. Lowe, M.D., Scientific Director

This Institute offers associate training programs in the ten branches indicated below. These programs include activities appropriate to a variety of specialized backgrounds, including obstetrics and gynecology, pediatrics, internal medicine and psychiatry, as well as physiology, biochemistry, biophysics, reproductive physiology, genetics, pharmacology, psychology, and developmental biology.

The Behavioral Biology Branch (Phillip G. Nelson, M.D., Ph. D., Chief) conducts electrophysiologic and biochemical studies of the neurobiologic basis for short- and long-term interaction between nerve cells. The central neural mechanism underlying sensory discrimination in primates is studied by electrophysiologic and behavioral techniques.

The Section on Brain and Behavior (David Symmes, Ph. D., Head). Electrophysiologic correlates of sensory coding and discriminative behavior are analyzed using microelectrode computer techniques. Behavioral consequences of brain lesions are studied.

The Section on Neurobiology (Phillip G. Nelson, M.D., Ph. D., Head). Tissue cultured neural and muscle tissue and small *in vitro* vertebrate and invertebrate neural systems are studied electrophysiologically and biochemically. Long-term interactions between neurons and between nerve and muscle are of particular interest.

The Children's Diagnostic and Study Branch (Charles U. Lowe, M.D., Acting Chief, and Duane Alexander, M.D., Project Head) is an outpatient facility where clinical research in biology, medicine, genetics, behavioral sciences, learning, communication, and epidemiology, as well as other types of investigations are carried out on children with physical, intellectual, behavioral, learning, or sensory handicaps. Both cross-sectional and longitudinal studies are utilized. Current topics of interest include an investigation of the cytogenetic, clinical, dermatoglyphic, and immunological findings in Down's syndrome among whites and Negroes; examination of prenatal factors which appear to influence psychobiological patterns displayed by the newborn infant; evaluation of the effect of maternal attitudes during pregnancy in relation to mothering behavior and infant development; the dynamics of counseling parents of mentally retarded children, including

"styles" of counselors and the familial factors which limit the counselor and the counseling; behavior modification through operant conditioning techniques; and acoustical analysis and perceptual study of voice in children with Down's syndrome.

A team consisting of pediatricians, social worker, public health nurse, psychologist, education specialist, neurologist, speech pathologist, audiologist, child psychiatrist, and geneticist evaluate children suspected of having problems in one of the following areas: (1) delayed development; (2) mental retardation; (3) perceptual motor, or sensory dysfunction; (4) communication disorders; (5) specific learning disability related to general insults such as prematurity, birth trauma, post-infectious states, or metabolic disorders.

Clinical and Research Associates as well as Staff Fellows participate in various clinical and research activities. Collaborative studies are carried out with other research facilities.

Developmental Biology Branch (Charles U. Lowe, M.D., Acting Chief). In this unit the normal and abnormal developmental aspects of cellular differentiation, tissue interaction and morphogenesis are investigated with the methods and within the conceptual framework of such disciplines as developmental biology, developmental pharmacology, experimental embryology and the development of behavior. Current studies range from the molecular level (investigations of the role of masked messenger RNA in induction and the developmental phenomenon of "determination") to the level at which normative base lines are established for human menstrual cycling and for the duration of human gestation. Between these two extremes, the brain, the inner ear and the eye are under intensive experimental analysis to determine the factors responsible for the emergence of orderly patterns during embryonic development.

The Laboratory of Biomedical Sciences (J. C. Robinson, M.D., Ph. D., Chief) conducts basic research in genetics, developmental enzymology, intermediary metabolism, physiological controls, and molecular structure.

The Section on Molecular Genetics (Head, Philip Leder, M.D.) is concerned with both the biochemical and physiologic aspects of the hereditary process. Current studies involve the use of bacteria and their viruses, as well as certain mammalian viruses, as model systems for the investigation of information flow for gene to messenger to protein. Particular emphasis is on the mechanism of protein biosynthesis and the regulatory genetics of the virus, lambda.

In the Section on Developmental Enzymology (Head, J. C. Robinson, M.D., Ph D.) primary interest centers on the identification and characterization of pregnancy-associated maternal blood plasma enzymes and proteins, the characterization of enzymes synthesized by the placenta, and an analysis of some of the factors involved in enzyme induction in the developing fetus.

Investigators in the Section on Intermediary Metabolism (Head, Gordon Guroff, Ph. D.) develop laboratory analogs of mental retardation through the use of specific chemical agents and enzyme inhibitors, investigate the biosynthesis and degradation of macromolecules in neural tissue, elucidate mechanisms of transport of small molecules into and out of the brain, evaluate the effects of excesses or deficiencies of intermediary metabolites on cellular differentiation and organogenesis (particularly of the brain), and develop screening procedures for enzyme defects in mental retardation.

The Section on Physiological Controls (Head, Walter H. Glinsmann, M.D.) conducts research on the hormonal control of metabolism at the cellular and organ levels of organization, the mechanism of hormonal induction of enzymes, the regulation of cell growth as mediated by nucleotide interconversions, and the developmental effects of inducing alterations of metabolism during specific periods of early development.

The Section on Molecular Structure (Head, Erhard Gross, Ph. D.) studies fundamental methods for the elucidation of the primary structure of biologically significant molecules, emphasizing automation of laboratory processes. It also engages in the isolation and characterization of cellular constituents, establishes structure-function relationships, and identifies chemical processes related to memory and learning.

The Social and Behavioral Sciences Branch (Leon Yarrow, Ph. D., Acting Chief) studies fundamental developmental processes including studies of cognitive, social and personality development, the interrelations among these functions, and the interactions between social-environmental and biological influences. These studies center around defining early environmental influences on development, and are concerned with both methodological and theoretical issues.

Current emphasis is on the earliest periods of development, i.e., infancy and preschool life with reference to early environmental influences on cognitive and personality developments. Research on infants in "disadvantaged environments" seeks to define the relations between specific aspects of early mother-infant interaction, e.g., sensory-perceptual stimulation, social-affectional components of maternal behavior and early cognitive and social development. Studies of preschool children, being carried out in Headstart schools and in varied middle class school environments, include several interrelated problems: development of methods for analyzing the complex learning environments of preschool children; study of the relations between various classes of teacher behavior, peer interaction, sensory stimulation and changes in cognitive and personality functions; the interrelations between cognitive and personality functions in preschool children, e.g., the relations between the growth of language and symbolic functions and the acquisition of impulse controls.

Reproduction Research Branch (William Tullner, Ph. D., Acting Chief) conducts an integrated program of clinical and biological studies concerning human and animal reproduction with emphasis on gonadal development, pubescence, ovulation, fertilization, implantation, menstruation and its disorders, pregnancy and its complications, sterility, and conceptual control.

Associates participate in basic animal studies or in correlated clinical investigations involving both inpatient and outpatient observation and care.

The multidisciplinary program of the Gerontology Research Center (Nathan W. Shock, Ph. D., Associate Scientific Director for Gerontology), located in a special research building on the campus of the Baltimore City Hospitals, offers Clinical (primarily clinical research) and Staff (primarily basic research) Associate training. Preference is given to candidates who intend to pursue careers in investigative and academic medicine. With appropriate approval, Associates may participate in clinical activities of the Baltimore City Hospitals and the nearby hospitals of the Johns Hopkins University and the University of Maryland. The Baltimore City Hospitals are affiliated with both institutions.

Associates participate in a seminar conducted by the staff of the Center which presents a comprehensive view of research in aging. Weekly research conferences are presented by members of the staff and invited lecturers.

In support of the programs in molecular aging and cellular and comparative physiology the Center maintains extensive animal colonies to provide rats, mice, hamsters, house flies, campanularia, rotifers, etc., of known ages, including senescent animals. Animal operating rooms are available as well as shops for the design and construction of special equipment. The library of the Center includes standard scientific journals as well as an extensive collection of the literature on aging research.

Since appointments are for 2 years, vacancies do not necessarily occur within each program area each year. For further information about any of the branches, candidates are encouraged to write Dr. Reubin Andres, Gerontology Research Center, NICHD, Baltimore City Hospitals, Baltimore, Md. 21224.

The Cellular and Comparative Physiology Branch (C. H. Barrows, Sc. D., Acting Chief) places primary emphasis on studies of age changes in cells and tissues of animals of different species. In this connection the effects of environmental factors on mortality and life span in different animal species are being investigated. The biological mechanisms involved in the increase in life span induced by reduced food intake is under study in a variety of animal species. In addition to physiological studies, morphological observations on the structure of cellular particulates, cells, and tissues are made using light microscopy, fluorescence microscopy, and electron micros-

copy. The aim of these studies is to correlate age changes in structure with function. The primary emphasis of the program is on the comparative physiology of aging.

In the Clinical Physiology Branch (Reubin Andres, M.D., Acting Chief) studies on age changes in organ systems and their integration are conducted with special reference to man. Major research efforts are conducted in a metabolism unit (hormonal control of carbohydrate metabolism), an endocrine unit (renin-angiotensin and thyroid physiology), a human performance unit (pulmonary and exercise physiology), and a cardiovascular-renal unit. The relation of physiologic age changes to specific disease states are conducted on a 38-bed research ward supervised by the staff of the Gerontology Research Center with the cooperation of the Department of Medicine and other clinical departments of the Baltimore City Hospitals. Studies are conducted on selected patients from the Baltimore City Hospitals and on a control group of over 600 community dwelling, active, healthy males (aged 20 to 100 years) who are volunteers in a prospective aging study. They spend 2½ days in the hospital every 18 months for detailed physiological and psychological tests. Although the major emphasis of the program of the Branch is on human studies, identification of the mechanisms of observed age changes involve animal experimetation as well.

The program of the Laboratory of Behavioral Sciences (Bernard T. Engel, Ph. D., Acting Chief) includes studies of the effects of aging on motor behavior, perceptual skills, learning, memory, problem solving ability and personality characteristics. There are also studies on the interrelationships among aging, autonomic regulation and behavior. The factors mediating learned control of autonomic responses, and the clinical applications of voluntary, autonomic control are being investigated. Laboratory facilities exist for measuring cognitive and perceptual functions in man; psychophysiological responses in man; learning and motor behavior in rodents (including selected in-bred strains of mice); learning, cardiovascular and neuropsychological responses in monkeys.

The Molecular Aging Branch (Bertram Sacktor, Ph. D., Chief) conducts research on the control of biochemical systems and metabolic pathways that show functional changes with age. Studied are enzymatic mechanisms regulating energy generation and transduction; inter- and intracellular transport of sugar, metabolites and ions; action of hormones in regulating intermediary metabolism; enzyme induction and the biogenesis of subcellular membranes and organelles; biochemical and ultrastructural localization of enzymes and metabolites; and regulation of glycogenolysis, glycolysis, gluconeogenesis, citric acid cycle activity, and oxidative phosphorylation.

Investigated also are the primary and conformational structure of DNA and RNA; the interactions of nucleic acids with each other, proteins and metal ions; and the expressions of these interactions in terms of biological function in relation to age. Correlations between physical properties, chemical composition, structure and function of connective tissues, blood vessels, skin and biomembranes are examined to evaluate alternations at the molecular level during aging.

National Institute of Dental Research

Richard C. Greulich, Ph. D., Director of Intramural Research

George E. Garrington, D.D.S., Deputy Director of Intramural Research (Clinical Investigations)

The National Institute of Dental Research conducts research programs in laboratory, clinical and applied science, germane not only to dental health but also to the broader interests of biology and medicine.

Physicians are appointed for a 2-year period to the Institute's laboratory or clinical programs as Research or Clinical Associates. In general, three Research Associate and two Clinical Associate positions are available annually. Specific program areas, however, will not necessarily have vacancies for Associates in a particular year.

For the most part, dentists will be appointed for 2 years as Dental Clinical Associates, with a dual commitment to research and service as described on page 3. Three or four Dental Clinical Associates will be selected annually. Dental graduates who possess specialized training and interests applicable to a particular research program of the Institute may also be considered for appointment as Staff Associates, with a full-time assignment to the appropriate laboratory or branch. The number of positions of this type to be filled will be determined solely according to programatic need, and will usually not exceed two per year.

Brief descriptions of the program areas to which Associate appointments are made are provided in the following paragraphs. Additional information about specific programs may be obtained upon request to the Director of Intramural Research, NIDR, National Institutes of Health, Bethesda, Md. 20014.

The Laboratory of Biochemistry (Karl A. Piez, Ph. D., Chief) conducts programs in basic research covering a broad range of biochemical topics. The laboratory has as its objective the investigation of fundamental biochemical processes in normal and disease states.

Research and Staff Associates are assigned to one of four sections according to the interest of the Associate: Protein Chemistry (Karl A. Piez, Ph. D., Chief), Connective Tissue Chemistry, (George R. Martin, Ph. D., Chief), Enzyme Chemistry (John E. Folk, Ph. D., Chief), or Cell Biology (Herbert L. Cooper, M.D., Chief). Ample opportunity is provided for interchange and collaboration between sections and with other groups at NIH.

Current research includes: chemical and physical chemical studies on proteins; the chemistry of crosslinks and the determination of amino acid sequences in collagen; the biosynthesis of collagen, elastin and other connective tissue components in animals and in tissue culture; the chemistry and mechanism of action of enzymes; the macromolecular events occurring in the cell prior to and during differentiation; and the chemistry and mechanism of action of muscle proteins.

The Laboratory of Microbiology (Stephan E. Mergenhagen, Ph. D., Chief) has as its broad objective the elucidation of the microbial ecology of the oral cavity, that is, to understand the interactions of members of the oral microbiota with one another and with the tissues of the host in which they reside, particularly in reference to oral and systemic health and disease. The broad basic programs in microbiology have application to medical and dental problems. Cooperative research with other laboratories is conducted as required by the interdisciplinary nature of particular projects.

The Virology Section (Abner Louis Notkins, M.D., Chief) is interested primarily in factors responsible for recurrent and persistent virus infections. Studies are being conducted on the effect of virus infections on the functional capacity of the immune system; the mechanism of neutralization of sensitized herpes simplex virus by antiviral antibody, antigamma globulin and the purified components of complement; factors responsible for the persistance of infectious virus and elevated enzymes in mice infected with lactic dehydrogenase virus; and cell fusion as a method for recovering infectious virus.

The Microbial Physiology Section (Charles L. Wittenberger, Ph. D., Chief) conducts research on mechanisms by which growth and biochemical activities of microbial cells are regulated, with a view to explaining physiological phenomena in molecular terms. Current studies are directed toward resolving the means by which lactic acid production by cariogenic streptococci is regulated. The pathways by which various organic compounds are fermented by this group of organisms is also being explored. In addition, comparative investigations on the genetics and metabolic activities of microorganisms are being pursued as part of a general approach to systematic microbiology.

The Immunology Section (Stephan E. Mergenhagen, Ph. D., Chief) is primarily involved in studies on the role of immunological mechanisms in oral and systemic disease. Current investigations are concerned with the immunobiological effects of endotoxins and other toxic products of microorganisms implicated in peridontal disease. The role of serum complement and "natural" antibodies in endotoxin-induced inflammation is being explored. Effects of lactic dehydrogenase virus and other adjuvants on immunological tolerance and the mechanism of tolerance at the cellular and subcellular level are being investigated. Studies are being carried out on immunosuppressive agents such as antilymphocyte serum and its mechanism of action in transplantation reactions.

The Laboratory of Biological Structure (Marie U. Nylen, D.D.S., Chief) is primarily concerned with structural parameters of normal and abnormal function as expressed at varying levels of biological organization, ranging from the subcellular to the organismic. Information is adduced from the application of biophysical and chemical methods, techniques of experimental embryology, as well as from relevant tools of modern histology.

Research and Staff Associates are appointed to the Laboratory and are assigned by mutual agreement to a preceptor in one of the following sections: Molecular Structure (E. D. Eanes, Ph. D., Chief); Growth and Differentiation (C. T. G. King, Ph. D., Chief); Biostructural Interractions (H. A. Bladen, Ph. D., Chief); and Experimental Morphology (M. U. Nylen, D.D.S., Chief).

Currently, the Laboratory is engaged in a broad series of structurally oriented projects. These relate to normal growth and differentiation, drug-induced developmental abnormality, the secretory process, crystal chemistry, and mineralized tissues, as well as to morphofunctional characteristics of whole and fractionated tissue cells, macromolecules, microorganisms and viruses. Opportunities for cooperative research and training are offered in electron microscopy and diffraction, contact and projection microradiography, X-ray diffraction, infrared absorption spectrophotometry, and cytochemistry.

The Laboratory of Physiology (Richard C. Greulich, Ph. D., Chief) has as its mission the execution of research programs broadly focusing on oral homeostatic mechanisms in health and disease. Emphasis is currently being placed on (1) the microbial ecology of the mouth; (2) integrated responses of the oral system as mediated by neural control; and (3) development of techniques for utilizing computer systems in experimentally monitoring and regulating the multiparametric factors which contribute to oral homeostasis. Experimental approaches derived from the disciplines of biochemistry, physiology, computer sciences and electronics play an essential role in these studies.

Specifically, the Environmental Mechanisms Section (Micah I. Krichevsky, Ph. D., Chief) investigates systems of controlled and uncontrolled interactions between a cell or group of cells and its environment. A primary aspect of these studies relates to the role of environmental cyclic or acyclic mononucleotides in cell interactions, especially those resulting in growth, chemotaxis, on structural differentiation.

Also under investigation is the response of caries-conducive streptococci to environmental parameters. Presently under study are: the dynamics of growth of these bacteria; their minimal nutritional requirements; the sequestration of phosphate (a main constituent of teeth) into the bacterial cell substance; the determinants of acquisition of capability of streptococci to adhere to surfaces; and, related to this last, the dynamics of accumulation of cell-associated polysaccharides.

The Neural Mechanisms Section (Ronald Dubner, D.D.S., Ph. D., Chief) conducts research on neural mechanisms in the oral and facial regions, especially those related to responses of the organism to its external environment. Current research topics include (1) peripheral and central neural mechanisms of orofacial sensation mediated by the trigeminal system, with particular emphasis on responses to tactile and noxious stimuli, and (2) sensory interaction in association areas of the cerebral cortex and the role of these cortical sites in higher cognitive functions of the brain. These research activities utilize conventional neurophysiological techniques of recording the electrical activity of individual cells in the brainstem and cerebral cortex and computer analysis of the temporal patterns of single-cell activity evoked by different somatic and visual stimuli. In addition, ultrastructural studies of the trigeminal brainstem nuclei are conducted in conjunction with neurophysiological studies of the trigeminal system.

The Experimental Pathology Branch (Harold M. Fullmer, D.D.S., Chief) conducts basic and applied research on a variety of diseases, especially those of major interest to dentistry. Metabolic studies of connective tissues hold a special interest.

The Histochemistry Section (Harold M. Fullmer, D.D.S., Chief) conducts histochemical, microchemical, biochemical and tissue culture studies of various oral and other tissues. Current studies include (1) the isolation, purification and characterization of collagenase from several sources, (2) the relation of collagenase, proline hydroxylase, and cross linking enzyme levels to various oral diseases, (3) the relation of hyaluronidase, beta glucuronidase, and beta glucosaminidase levels to oral diseases, (4) histochemical studies of bone resorption, developing teeth and of various oral disease conditions, and (5) studies of factors in the oral environment that promote degradation of the oral tissues in periodontal diseases.

The Diagnostic Pathology Section (Howell Archard, D.D.S., Chief) is concerned with the operation of a diagnostic oral pathology service. An accredited residency training program in oral pathology is also offered.

The Experimental Oncology Section (James E. Hamner III, D.D.S., Ph. D., Chief) is concerned with histopathologic studies of oral disease in man and in animals. Current studies include histopathologic studies of tissue reactions to synthetic implants, and experimental oral tumors in animals.

The Human Genetics Branch (Jerry D. Niswander, D.D.S., Chief) conducts projects in experimental, clinical, and population genetics, with the objective of elucidating the genetic mechanisms in various diseases and normative traits. A variety of approaches ranging from biochemical to mathematical as well as clinical skills in both medicine and dentistry are utilized. The program of the branch is implemented by two sections.

The Developmental Genetics Section (Kenneth S. Brown, M.D., Chief) studies normal and abnormal traits of man and experimental animals with a view to determining the nature of the developmental processes involved, and the degree to which these are under genetic control. Experimen-

tal embryology is used to determine the nature of developmental processes that result in structural variations of the face and dentition. Morphologic anomalies of the dentition are studied histologically in combination with breeding experiments. Variation in human taste and smell perception is investigated to determine the nature of the receptor processes and their degree of genetic control. Genetic variation in the physiologic and biochemical properties of saliva is also under study.

The Population Genetics Section (Jerry D. Niswander, D.D.S., Chief) conducts field and laboratory studies of congenital malformation, malocclusion, and dental variation in different populations. Microdifferentiation in human populations (particularly American Indian groups) is also a major area of concern. Investigations include the effects of natural selection and inbreeding, as well as other factors affecting mating pattern on the genetic structure and disease patterns of different groups. A major source of data for this work is obtained from red cell and serum typing conducted within the Branch.

The Biometry and Field Investigations Branch (James P. Carlos, D.D.S., Chief) is concerned with the study of the occurrence of oral diseases in relation to various characteristics of the persons examined, their way of life, and the environment in which they live. Field studies are designed and conducted in an effort to identify, within this dynamic complex, variables which influence favorably or unfavorably the occurrence of disease. The objective of epidemiological study is to provide information that might prove useful in the prevention, control or treatment of disease.

Research activity of the Branch is currently devoted to the epidemiological study of dental caries, periodontal disease, and occlusion, which represent by far the 3 most prevalent problems of oral health. Work is undertaken collaboratively within the Branch, and usually also involves participation of other units of the Institute, especially the Dental Services Branch.

The Clinical Trials Section (H. R. Englander, D.D.S., Chief) conducts laboratory and field studies of agents thought to have potential for the prevention and control of dental and oral diseases.

The Biometry Section (James P. Carlos, D.D.S., Chief) provides statistical and data processing consultation to Institute and other dental scientists, and conducts a research program in the methodology of design and analysis in oral research.

Investigations presently being conducted by the Branch are especially concerned with: (1) the role of dental plaque in the causation of dental caries and periodontal disease; (2) evaluation of new therapeutic measures directed against caries and periodontal disease; (3) assessment of the prevalence and severity of malocclusion in terms of newer epidemiological methods of diagnosis and scoring; and (4) the role of trace nutrients, other than fluoride, in enhancing oral health.

The Oral Medicine and Surgery Branch (George E. Garrington, D.D.S., Acting Chief) provides the specialty staff for the conduct and

support of clinical investigations, both inpatient and outpatient, relating to oral disease. Etiologic and therapeutic investigations undertaken within the Branch reflect the variety of interests among its physicians and dentists: periodontology, orthodontics, oral surgery, oral pathology, and the interrelationships of oral disease and systemic disease. In addition to its broad support of clinical investigations in these areas, the Branch has three discrete research units, each of which has specific focus on problems of relevance to biomedical endeavor generally.

1. The Oral Pharyngeal Development Section (James F. Bosma, M.D., Chief) is concerned with the development of form and of respiratory and feeding functions in normal and in impaired infants and children. The staff of physicians and dentists collaborates in study and therapy of inpatients and outpatients. Study methods commonly include standard and cephalometric radiology, cinephotography, and speech recording. Particular efforts are made to adapt familiar study techniques and therapies to patients severely handicapped by anomaly or neurological impairment.

2. The Anesthesiology Section (Edward J. Driscoll, D.D.S., Chief) is responsible for the broad area of research in pain control for all dental operations. Physiologic studies on patients undergoing dental and oral surgical procedures under both general and local anesthesia are the subject of present interest. All the readily measurable physiological parameters such as blood pressure, pulse, EKG, EEG, arterial oxygen saturation, $_pCO_2$, etc., which can be managed in an outpatient system are being investigated.

The correlation of significant anesthetic and surgical events, such as the amount and type of drug, depth of anesthesia, and type and duration of surgical stimulation, with physiologic alterations are an integral part of the study.

3. The Protein Structure and Immunochemistry Project (Norman A. Cummings, M.D., Project Leader) is concerned with the study of protein structure and behavior related to various connective tissue disorders. Both laboratory and clinical studies are carried out on such diseases as Behcet's syndrome, scleroderma, systemic lupus erythematosus, and Sjögren's syndrome. Emphasis is placed upon the study of rheumatoid arthritis and its effect upon oral function through temporomandibular joint involvement.

The Dental Services Branch (Samuel Kakehashi, D.D.S., Chief) has as its prime function the dual responsibility of providing dental care to the NIH-wide research patient population as well as of providing facilities and supportive activity to all intra-Institute clinical programs. This patient exposure provides a unique opportunity for gaining experience in the observation, treatment, and study of orofacial problems related to a variety of systemic disease. All Dental Clinical Associates are assigned to this Branch administratively so as to facilitate their service-related activities. However, an individual program is arranged for each Associate in order that he may also pursue effectively his clinical and/or basic research interests.

National Institute of Environmental Health Sciences

Paul Kotin, M.D., Director

William W. Payne, Sc. D., Deputy Director

Hans L. Falk, Ph. D., Associate Director for Laboratory Research

General

The mission of the National Institute of Environmental Health Sciences (NIEHS) is to identify the chemical, physical, and biological factors in the environment that can adversely affect man; to contribute to an understanding of the mechanisms and manifestations of human diseases produced by these agents; and to provide the scientific basis for the development of control measures by other agencies. NIEHS is particularly concerned with the effects of agents at low concentrations acting over long periods; the interaction of multiple agents resulting in enhanced effects; and the modifying effects of variable physical and biological states within man on susceptibility to and course of disease induced by these agents.

There is no single discipline that is unique or specific for the study of environmental health problems. Rather, the distinctive requirement for such research involves the application of a spectrum of skills including biology, biochemistry, bioengineering, biometry and epidemiology, chemistry, pathology, pharmacology, physics, toxicology, and veterinary sciences.

Location

The headquarters and intramural research programs of NIEHS are located at the National Environmental Health Sciences Center (NEHSC) in Research Triangle Park, N.C. The National Institute of Environmental Health Sciences is the only one of the 10 Institutes comprising the National Institutes of Health to be located away from the Bethesda, Md., campus.

Proximity to three universities—the University of North Carolina at Chapel Hill, Duke University at Durham, and North Carolina State University at Raleigh—has encouraged the development of a close working relationship between the staffs of the universities and the Institute. This relationship affords the NIEHS staff access to extensive library facilities as well as opportunities to participate in teaching, in seminars, and in other scientific and professional activities associated with the universities.

Staff Associates

Staff Associates will work at the National Environmental Health Sciences Center under the direction of Dr. Paul Kotin, Director, and Dr. Hans L. Falk, Associate Director for Laboratory Research. Each Associate will work directly under a senior scientist in an area of research chosen by the Associate and the Institute.

The Analytical and Synthetic Chemistry Branch (Lawrence Fishbein, Ph. D., Chief) supports programs designed to conduct and augment research related to the effects of a broad spectrum of environmental agents (pesticides, food additives and contaminants, trace metals, and pollutants of air and water—including also their metabolic and degradation products). The program also includes the elaboration of environmental parameters (ultraviolet, ozone, and thermal) on the stability of diverse pesticides and related derivatives; the analysis of multiple components in the elaboration of synergistic effects; the development or improvement and standardization of analytical techniques for the determination of specific chemicals; and the preparation of required intermediates for confirmation of identity of metabolites and degradation products through synthetic procedures. Research studies by the Branch include the separation and identification of components of essential oils, the study of biliary and urinary metabolites following administration of pesticide synergists and other toxicants, and the determination of the effects of aflatoxin excreted in the milk of rats on the development of their offspring.

The Animal Science and Technology Branch (John A. Moore, D.V.M., Chief) is responsible for the acquisition, quarantine, and conditioning of all biological models for the NEHSC; for the maintenance, husbandry, and veterinary care of all experimental colonies utilized by the NEHSC; for special services relating to the animal sciences; and for the conduct of a broad but meaningful research program consistent with the mission of the Center. Individual scientists on the Animal Science and Technology Branch (ASTB) staff conduct related research programs within the scope of their professional disciplines as a part of the overall NEHSC mission and ASTB research programs. These programs include a study of the effects of acute and chronic exposure to pesticides and other organic compounds and studies of the effect of photoperiod, light intensity, and exposure to various spectral wavelengths on reproductive physiology.

The Cell Biology Branch (Robert G. Owens, Ph. D., Chief) seeks to clarify the long-range effects of noxious environmental agents on cells and tissues, to elucidate the fundamental mode of action of such agents, and to assess the significance of toxicant-induced malfunctioning after long-term exposure on the long-range health of man. Research currently underway includes investigation of the induction of mitochondrial defects by toxic agents, effects of alkylating and other types of environmental agents on metabolism, enzyme induction by xenobiotic compounds, and the long-range

effects of mutagenic compounds on the mammalian genome and on gene repair. Important advances are being made toward characterizing the effects of toxins on ribosomes and on polysome integrity in relation to protein synthesis by use of mammalian tissue cultures. The distribution and potential importance of new mycotoxins in the environment are being explored. The fate and mode of action of these toxins in the animal body are being studied along with the enzyme systems responsible for detoxifying these substances and eliminating them from the body.

The Pathologic Physiology Branch (William Jurgelsky, M.D., Ph. D., Acting Chief) is concerned with the identification of environmental toxicants and the elucidation of their toxic mechanisms at the organ, cellular, and subcellular levels. Correlations are being sought between toxicant-induced changes in mammalian structure, as visualized by light and electron microscopy, and corresponding changes in function, as revealed by techniques of biochemistry and physiology. Work is in progress on the acute and chronic effects of the nervous and endocrine systems of a variety of chemicals and environmental pollutants, individually and in combination. Experimental lipidoses, and epilepsy, demyelination, and experimental thyroiditis are current areas of interest. The carcinogenic potential to the neonate marsupial of selected pesticides, heavy metals, and other agents is also under investigation. The marsupial is being utilized as a primary biological model in many of the studies underway.

The goals of the Pharmacology and Toxicology Branch (Herbert S. Posner, Ph. D., Acting Chief) are to identify the effects of selected environmental chemicals on the processes of growth and development and on normal tissue function, in general, both in the young and in the adult. With respect to growth and development, both teratogenesis and abnormal growth in their broadest senses are being considered. With respect to the young and the adult organism, effects on selected organs and organ systems, as for example on the lung, cardiovascular, and nervous systems, are being probed. Delayed and chronic effects are given preferential consideration, while the agents are considered singly or in combination. Finally, the mechanisms of development of the responses obtained and the factors which may distinguish or, alternatively, allow a correlation between the responses of experimental animals and humans are sought.

National Institute of General Medical Sciences

Bryon B. Clark, Ph. D., Director, Pharmacology-Toxicology Program

George J. Cosmides, Ph. D., Coordinator,

Pharmacology-Toxicology Program

Pharmacology Research Associates

This Institute will select at least two Pharmacology Research Associates for 1971. Those who are appointed will receive 2 years of postdoctoral training in a laboratory of a participating Institute of the National Institutes of Health under the Pharmacology Research Associate Training Program.

The program is directed to those who have already made a commitment in pharmacology by training or research in the field.

Associates will study principles of pharmacology and toxicology and the application of physical and chemical concepts to pharmacology. Training in such areas as applied mathematics, biometrics, organic chemistry, biochemistry, physics, and instrumentation is also available. During their tenure, pharmacology research associates devote the larger portion of their time to laboratory research in the biomedical sciences, with no clinical responsibilities.

The purpose of this training is to develop leaders in pharmacology research for key positions in academic, industrial, and governmental research laboratories.

Professional growth is achieved through the process of personal guidance by senior NIH scientists, chosen by mutual selection, coupled with a variety of laboratory problems and many different research approaches, designed to advance both the work in progress and the competence of the prospective independent investigator.

Candidates who need experience in pharmacology and wish to broaden their experience in biomedical sciences may make their selection from the following program areas (also see Program Area Selection Check List, which is page 8 of the application):

National Cancer Institute

Cancer Chemotherapy National Service Center
Dr. Abraham Goldin (chemotherapy)

Laboratory of Chemical Pharmacology
Dr. David P. Rall (chemical pharmacology)
Dr. Vincent Oliverio (biochemical pharmacology)
Dr. Richard H. Adamson (drug metabolism)
Laboratory of Physiology
Dr. Marco Rabinovitz (protein biosynthesis and antimetabolites)
Chemistry Branch
Dr. Harry V. Gelboin (enzyme induction and carcinogen metabolism)

National Heart and Lung Institute
Laboratory of Biochemical Genetics
Dr. Marshall Nirenberg (molecular biology)
Cardiology Branch
Dr. Stephen E. Epstein (circulatory physiology)
Laboratory of Chemical Pharmacology
Dr. Bernard B. Brodie (mechanisms of drug action)
Dr. James R. Gillette (enzymes drug interaction)
Dr. Elwood Titus (drug and transport mechanism)
Laboratory of Molecular Diseases
Dr. Martha Vaughan (hormonal control of lipolysis)
Experimental Therapeutics Branch
Dr. Albert Sjoerdsma (experimental therapeutics)

National Institute of Allergy and Infectious Diseases
Laboratory of Parasitic Diseases
Dr. Eugene Weinbach (interactions of drugs with mitochondria)

National Institute of Arthritis and Metabolic Diseases
Arthritis and Rheumatism Branch
Dr. Peter Goldman (biochemical pharmacology)
Laboratory of Biochemical Pharmacology
Dr. Herbert Tabor (biochemical pharmacology)
Laboratory of Chemistry
Dr. John W. Daly (biogenic amines and enzymatic hydroxylation)

National Institute of Dental Research
Laboratory of Biological Structure
Dr. C. T. G. King (drug-induced malformations)

National Institute of Mental Health
Laboratory of Clinical Science
Dr. Julius Axelrod (pharmacology)
Dr. Irwin J. Kopin (medicine)
Laboratory of Cerebral Metabolism
Dr. Louis Sokoloff (cerebral metabolism)
Laboratory of Preclinical Pharmacology
Dr. Erminio Costa (preclinical pharmacology)
Laboratory of Neuropharmacology
Dr. Floyd E. Bloom (neuropharmacology)

National Institute of Mental Health

John C. Eberhart, Ph. D., Director of Intramural Research

Robert A. Cohen, M.D., Ph. D., Director of Clinical Investigations

This Institute offers an opportunity for post-doctoral research training in psychiatry and in the biological and behavioral sciences. Clinical Associates are usually assigned clinical and research responsibility with approximately one-half time for each endeavor. However, specific arrangements including time allocations, vary in the different Branches and Laboratories. Staff Associates engage in laboratory research in one of the biological or behavioral science laboratories under the preceptorship of one of the senior staff, and may in addition participate in tutorial seminars and other teaching programs, as their needs and desires indicate. After reporting for duty certain Staff Associates who have particular need for and interest in the tutorial seminar program, and whose qualifications are high, may be designated as Research Associates, and will be given priority in admission to the seminar programs.

Most Staff Associate appointments will not involve deferment for residency training under the CORD program. However, an occasional CORD deferment may be available for Staff Associates whose research duties require that they have 1 or more years of residency training.

Lectures, seminars, and group discussion by members of the staff and by visiting lecturers complement the training program, making it possible for Associates to acquire a broad background in the neural and behavioral sciences with more intensive and individualized study in selected aspects of the field.

It should be noted that clinical experience in the NIMH emphasizes the opportunity to learn to use a ward and its staff for research purposes as well as for treatment. An opportunity is provided to administer a research ward for the treatment of psychiatric patients emphasizing community oriented milieu therapy and utilizing various patient and patient-family groups as the major therapeutic instruments.

Descriptions of the NIMH program areas to which Associates will be appointed follow.

The Adult Psychiatry Branch (Lyman C. Wynne, M.D., Ph. D., Chief) conducts a broad program of psychiatric research, clinical care, specialized clinical training and psychiatric research training. Ordinarily, 2 or 3 years of clinical psychiatric residency training should precede arrival

on duty; for Clinical Associates, the program is accredited for third-year psychiatric residency training. Candidates for Clinical Associate appointment ordinarily should apply for the year which is either 3 or 4 years after graduation from medical school (counting 1 year internship and 2–3 years psychiatric residency).

Associates are appointed to the branch as a whole. However, later on, when coming on duty, the Associate will be assigned to a particular section and senior staff preceptor within the branch, in accord with the nature of branch activities and when possible, the Associate's interests and experience at that date.

The branch is administratively organized into the Office of the Chief and seven sections. In all of these sections which conduct psychiatric treatment, the clinical work emphasizes a psychodynamic approach, especially family psychotherapy with adolescents and their families. Research projects currently include studies of: (1) links between family communication and psychopathology of offspring (Dr. Lyman Wynne and others); (2) adolescent identity crises and their treatment in the family context (Drs. Roger Shapiro and John Zinner); (3) genetically identical twins discordant for schizophrenia and their families (Dr. William Pollin); (4) criteria for longitudinal predictions and therapy of adolescents and their families (Dr. Helm Stierlin); (5) relationships between verbal and perceptual aspects of behavior (Dr. Winfield Scott); (6) cross-culturally standardized approaches to assessment of psychotic patients (Drs. John Strauss and W. T. Carpenter); (7) experimental studies of interaction in families and small groups (Dr. David Reiss); and (8) attentional, perceptual, and neurophysiologic variables in schizophrenia and altered states of consciousness (Dr. Lyman Wynne).

The Laboratory of Clinical Science (Irwin J. Kopin, M.D., Chief. Senior Staff: Dr. Julius Axelrod, Dr. Ira B. Black, Dr. William E. Bunney, Jr., Dr. Philippe V. Cardon, Dr. Thomas N. Chase, Dr. John F. Davis, Dr. Edward V. Evarts, Dr. Frederick K. Goodwin, Dr. Dennis Murphy) conducts a program of research in biochemistry, pharmacology, physiology, medicine and psychiatry and the interrelationships between them. Current research includes: (1) mechanism of action and metabolism of drugs and hormones which act in the nervous system, especially catecholamines; (2) biochemical studies in endocrine and metabolic disorders of amino acids, catecholamines and other biogenic amines; (3) unit activity in cortical and subcortical areas in relation to sleep and attention; (4) circulatory physiology and psychosomatic medicine; (5) longitudinal investigation of patients (acute or episodic psychosis, depression) stressing biological factors (endocrine function, catecholamines, serum proteins, specific enzyme activities); (6) biological rhythms and their control; (7) biological aspects of toxic psychoses; and (8) drug metabolism.

The Laboratory of Neurobiology (Ichiji Tasaki, M.D., Chief) conducts research on the nervous system at several levels ranging from biochemical and biophysical studies of single excitable cells to studies of systems of neurons in the brain. Current research projects include studies on: (1) the excitation process in nerve and muscle membrane using recently developed optical techniques to demonstrate changes in birefringence turbidity, and fluorescence in excitable tissue during an action potential; (2) protein synthesis in neuronal cell nuclei in an attempt to define biochemical characteristics of neurons which may relate to their function as long-lived dividing cells; and (3) the integration in the brain of visual information and extravisual input (such as eye movements and attention) using single unit recording in awake monkeys performing a learned task.

The Laboratory of General and Comparative Biochemistry (Giulio L. Cantoni, M.D., Chief) conducts investigations on: Mechanisms and pathways of protein biosynthesis; biological methylations; and alkaloid biosynthesis.

The main focus of the laboratory is on the molecular biology of tRNA including determination of the base sequence of purified tRNAs, interaction with messenger RNA and ribosomal particles, biological coding, enzymology of tRNA, physicochemical studies, etc.

The Section on Alkaloid Biosynthesis studies the enzymes involved in alkaloid biosynthesis, their control and biosynthesis in relation to morphogenetic development of the plant; also, enzymatic mechanisms of transmethylation and intermediary metabolism of sulfur-containing amino acids in various conditions.

The Laboratory of Cerebral Metabolism (Louis Sokoloff, M.D., Chief. Senior Staff: Dr. Jack Durell and Dr. Marian W. Kies) conducts a program of research on: (1) chemistry of membranes; and mechanism of action of acetylcholine; (2) biochemical and immunochemical studies on myelin; and characterization of CNS proteins and their relationship in autosensitization reactions of the CNS; and (3) biochemistry of the developing nervous system; and effect of thyroxine and other hormones on protein synthesis.

The Laboratory of Neurochemistry (Seymour Kaufman, Ph. D., Chief) conducts investigations in the following areas: (1) the mode of regulation and the mechanism of action of a group of oxidative enzymes called oxygenases. The enzymes currently under study include phenylalanine hydroxylase, tyrosine hydroxylase and dopamine β-hydroxylase; the study includes an investigation at the molecular level of the enzyme defect in phenylketonuria and hyperphenylalaninemia; (2) the biochemical basis for skeletal muscle hypertrophy including the effects of exercise and neural factors in the process; (3) cell surface membrane proteins and their role in cellular differentiation; (4) DNA repair mechanisms and their role in aging; (5) the structure of viral DNA especially in relation to the phenomena of integration of viral DNA into host structures and viral transduction of host genes; (6)

electronic structure of DNA and its components with emphasis on specific interactions of nucleotides in cellular processes such as codon-anticodon recognition and DNA replication.

The Laboratory of Clinical Psychobiology (Frederick Snyder, M.D., Chief) conducts research on psychobiological relationships of possible psychiatric significance by means of experimental studies of normal humans and animals as well as intensive longitudinal studies of psychiatric patients. The general objective is that of promoting especially close interaction between clinical, experimental and comparative zoological investigation, pursuing each as far as possible in terms of measurable biological correlates of behavioral dimensions, and viewing human adaptation or maladaptation from a broad, ethological perspective. Current efforts take their principal point of departure from the electrophysiological study of sleep, attempting to explore the ramifications of that phenomenon in relation to (1) waking arousal and anxiety; (2) the natural history of acute depressive and schizophrenic psychosis; and (3) the evolutionary history of mammals.

Clinical Associates are involved in observation and treatment of a wide variety of patients while also having the opportunity to share in experimental studies within the laboratory. Consideration for a limited number of Research Associate positions will be given to those especially interested in laboratory assignments, but who wish to maintain some degree of clinical involvement.

The Laboratory of Neurophysiology (Wade H. Marshall, Ph. D., Chief) conducts a program in basic neurophysiology on problems ranging from basic membrane mechanisms to brain and behavior. Current investigations include (1) Brain and behavior with particular emphasis on the limbic system; (2) physiology and biophysics of membrane; (3) a program on simple nervous systems such as the *Aplysia;* and (4) general neurophysiology of the brain.

The Laboratory of Psychology (David Rosenthal, Ph. D., Chief) conducts investigations in eight broad research areas: (1) brain function in primates—cortical mechanisms in sensation and perception in the visual, auditory, and somesthetic systems; cortical mechanisms in problem solving; cortical-subcortical relations in the regulation of behavior; (2) evoked potential and sensori-perceptual studies in humans—exploration of relationships between perceptual response patterns, psychiatric clinical dimensions and neurophysiological measures; (3) etiological studies of schizophrenia with designs to investigate the genetic component of the disease—children of schizophrenics adopted by non-schizophrenic parents are evaluated for psychopathology by using psychological, psychiatric and psychophysiological techniques—comparing biological and adoptive parents of schizophrenic children as they are consecutively admitted to a psychiatric facility; (4) developmental and comparative psychology—parametric studies of early

learning and motivation in human infancy and childhood; modification of caretaking acts and general environmental conditions and their effects on infant and child behavior; effects of stimulation on behavioral development of infants and children; perceptual development and concept formation without verbal assistance in infants and preschool children; (5) biopsychology of learning and motivation—comparative analysis of behavior in neonatal dog, cat, and other mammals; (6) perception, thinking, and problem solving—effects of experimental procedures on time estimation in normals and schizophrenics; ways of increasing efficiency of solving complex cognitive problems; (7) communication—units of syntactic encoding and decoding in conversational speech; frequency of body movements as emotional expression; (8) the creative scientist—the effects of personality, environment and cognitive abilities on creative performance of young as well as mature scientists; longitudinal studies of a potentially creative sample.

The Division of Special Mental Health Research (G. C. Salmoiraghi, M.D., Ph. D., Director), located at Saint Elizabeths Hospital, (1) plans and conducts a program of intramural research on special mental health problems such as psychopharmacology, neuropharmacology, drug abuse, and the biochemistry of learning; and (2) provides policy guidance, technical direction, and logistical support to other special Institute research activities in areas such as crime and delinquency, alcoholism, and suicide.

The Laboratory of Clinical Psychopharmacology (Roger K. McDonald, M.D., Chief) conducts research primarily concerned with the mechanism of action of drugs which are relevant to behavior. Within a neurobehavioral frame of reference psychotropic drug actions are evaluated using one or more of the following approaches: neurochemistry, biochemistry, pharmacology, neurophysiology, physiology, animal behavior and clinical studies. Associated with the laboratories are extensive animal facilities available for acute and chronic metabolic and behavioral studies. In addition there is a research ward consisting of a 10-bed service and a six-bed intensive care and study unit. Both patients and normal volunteers are studied in the clinical facilities. Because the Laboratory of Clinical Psychopharmacology consists of both laboratory and clinical research operations, applicants should specify their area of interest.

The Laboratory of Neuoropharmacology (F. E. Bloom, M.D., Acting Chief) conducts a multidisciplinary research program centered upon the identification of synaptic transmitter substances, and the mechanisms by which neuro-active and psycho-active drugs exhibit effects upon synaptic transmission. The approach is entirely at the cellular level, utilizing intracellular and extracellular electrophysiologic techniques, micromethods of drug administration incuding microelectrophoresis, and cytochemical studies with light, fluorescence and electron microscopy. Specifically, studies are currenty being carried out on: (1) the characterization and pharmacology of potential monoamine-containing neuronal pathways in the mam-

malian central nervous system; (2) the relation between pharmacological responsiveness and development of structurally specialized synapses; and (3) the cytologic and physiologic organization of molluscan ganglia.

The Laboratory of Preclinical Pharmacology (E. Costa, M.D., Chief. Senior Staff: Dr. David Boullin, Dr. Norton H. Neff, and Dr. Benjamin Weiss) conducts a program of research in neurochemistry and neuropharmacology to elucidate chemical and physiochemical factors involved in the clinical response of drugs affecting neuronal function. Current research includes: (1) nature of postjunctional receptors with particular regard to the biochemical reactions occurring at the neuroeffector junction in response to adrenergic neuro-transmission; (2) rate-limiting enzymatic reactions controlling the dynamic equilibrium of metabolic compartments of neuronal monoamines; (3) regulation of acetylcholine metabolism in synapses in relation to changes of neuronal function; (4) human blood platelets as a model for pharmacodynamic studies; and (5) physiological and biochemical mechanisms of drug toxicity.

National Institute of Neurological Diseases and Stroke

Edward F. MacNichol, Ph. D., Director

General. The National Institute of Neurological Diseases and Stroke conducts, fosters, and coordinates research on the causes, prevention, diagnosis, and treatment of neurological and sensory disorders and related fields, and administers a program of research and training grants and awards.

Throughout the Institute, opportunities also exist for clinical and professional education, including many scientific disciplines.

CORD deferments for approved clinical training beyond a year of internship are available for some Clinical Associate positions in the clinical branches. Research and Staff Associate positions do not provide CORD deferments in this Institute. It is to be noted that Clinical appointments can be made for 2 or 3 years.

Intramural Research Program

Henry G. Wagner, M.D., Director
Maitland Baldwin, M.D., Clinical Director

The Medical Neurology Branch (W. King Engel, M.D., Chief) has as its major function the application of basic research techniques to the investigation of clinical neurological problems. The Clinical Associate becomes acquainted with a majority of the neurological diseases, with particular emphasis on the disorders of muscle, myasthenia gravis, lower motor neuron diseases, metabolic abnormalities of the central nervous system, and genetically determined disorders. He receives instruction in clinical neurology and the related clinical and basic sciences while developing an understanding of the various laboratory techniques which support the neurological investigation. During the first 12 months he is in a ward environment and is responsible for the care of patients on the Medical Neurology Service and the integration of related research. He covers the neurologic consultations to the other clinical services during 3 of those months. During the first year he is expected to learn to perform one of a variety of basic laboratory techniques (such as histochemistry, tissue culture, biochemistry, electron microscopy,

immunology, or electromyography) as it applies to a clinical problem. The second year is spent in full-time work on that clinical research technique. Some Clinical Associates may stay a third year to continue their clinical research activities.

The Surgical Neurology Branch (Maitland Baldwin, M.D., Chief) is concerned with the investigation of epilepsy, involuntary movements, head injury, developmental disorders, brain tumor, cerebral edema, effects of surgical lesions on the nervous system, psychological assessment of surgical lesions, the application of anesthesia to neurological disease states, and problems of hypothermia as related to the nervous system.

The Clinical Associate is required to study and has responsibility for the care of patients with epilepsy, involuntary movements, brain tumors, vascular malformations of the nervous system, and others with a miscellany of neurological disease. He receives practice and instruction in clinical neurology, and, in particular, in the diagnostic techniques of surgical neurology and the operative techniques of neurological surgery as well as the principles on which these techniques are based. He attends clinical rounds in Medical Neurology, staff conferences in electroencephalography and X-ray diagnosis, as well as neuropathological conferences. He is advised to acquire as great a familiarity with the various laboratory techniques as is commensurate with his individual responsibilities and the commitments of the various laboratories in the NINDS.

The Electroencephalography Branch (Cosimo Ajmone Marsan, M.D., Chief) involves a relatively small highly specialized patient population from the entire Clinical Center. The position of Clinical Associate is for a 2- or 3-year appointment (preference is given to persons with basic neurological training). In neurophysiology the appointment is also for 2 or 3 years (preference is given to people with some previous experience in the field of electrophysiology and a knowledge of neuroanatomy). Current research: Experimental epilepsy, thalamo-cortical relationship, nature of brain waves, microelectrode study of cortical neurons, etc.

Laboratory of Neurochemistry (Donald B. Tower, M.D., Ph. D., Chief) directs research toward the elucidation of the chemical attributes of neural tissues which underlie the normal functioning of the nervous system and the derangements of function in various neurological diseases. The investigations, which are primarily at the basic level, are distributed among four sections of the laboratory: the Lipid Chemistry Section (Head, Dr. R. O. Brady), the Enzyme Chemistry Section (Head, Dr. R. W. Albers), the Section on Amino Acids and Electrolytes (Head, Dr. D. B. Tower), and the Physiology and Metabolism Section (Head, Dr. E. G. Trams). In these investigations a wide variety of disciplinary approaches and methodologies, including appropriate clinical material, are being utilized. Special emphasis is given to the relevance of the various laboratory programs to neurophysiological problems, such as mechanisms subserving reception, conduction and

transmission of nerve impulses, and to clinical problems, such as the bases for the lipodystrophies, demyelinating diseases, epilepsy, cerebral edema, and nutritional and genetically-determined disorders.

The Laboratory of Molecular Biology (Ernst Freese, Ph. D., Chief) examines control mechanisms of RNA and membrane synthesis of transport and of differentiation by a combination of genetic and biochemical techniques. Candidates with a M.D. or Ph. D. are accepted.

Bacteria are used as the simplest cellular system. To determine the biochemical reactions involved in transport, sporulation and germination, mutants are isolated and characterized structurally, by microscopic and electron microscopic techniques, genetically by transduction and transformation, and biochemically, by radioactive measurements, isolation and assays of enzymes, thin-layer and gas chromatography, etc. The biochemical reaction involved in control and development during the commitment period are thus determined.

The Laboratory of Neuropathology and Neuroanatomical Sciences (Igor Klatzo, M.D., Chief) recognizes scientific advantages to be derived from close contact and interaction between various approaches used in the fields of neuropathology and neuroanatomical sciences. Thus investigations on basic pathogenic mechanisms operative in various neuropathological conditions are carried out parallel with or supported by studies elucidating structural and functional features of the normal nervous system. Specific problems under current investigation are: Effects of oxygen deprivation, edema, radiation on the brain, role of the glia, development and pathology of myelin, aspects of vascular permeability and transport mechanisms in the brain, mechanisms of neurohormonal regulation, localization of catecholamines, elucidation of some of the sensory and motor systems, investigation on normal structure and pathologic reactions in a primitive nervous system such as that of the Elasmobranchs. The main technical approaches include light and electron microscopy, histochemistry, radioisotopic and biochemical assays. The Laboratory is divided into six sections: (1) The Section of Functional Neuroanatomy, (2) The Section on Trophic Nerve Function, (3) The Section on Neurocytology, (4) The Section on Experimental Neuropathology, (5) The Section on Comparative Neuropathology, and (6) The Section on Cellular Neuropathology.

The Laboratory of Neurophysiology (M. G. F. Fuortes, M.D., Chief) conducts research on basic properties of nerve cells and on the organization of the nervous system. The *morphology* of cells, synapses and subcellular structures is studied by means of optical and electron microscopy. *Membrane properties* of receptor cells and central neurons are investigated. Studies on *receptor functions* include analysis of the responses of visual cells to light as well as kinetic studies aimed at determining the properties of the processes leading to the response. The properties of *central neurons and synapses* are studied in simple preparations derived from vertebrates and invertebrates.

Electrical and chemical properties of cells in *tissue culture* are also being investigated.

The Laboratory of Experimental Neurology (William F. Caveness, M.D., Chief) includes the following activities: (1) the investigation of the delayed effects of X-irradiation on the visual cortex of the Macaca mulatta utilizing an evoked response from photic stimulation, at successive intervals following exposure. The functional alterations are correlated with alterations in the five structures of the cortex; (2) ontogeny of focal seizures in the Macaca mulatta; (3) the investigation of the origin and development of the principal electrical patterns in sleep by surface and depth recording at successive age levels in the Macaca mulatta.

One Associate position is available for 2 to 3 years. Previous experience in electrophysiology or neuroanatomy would be an advantage.

The Laboratory of Neural Control (Karl Frank, Ph. D., Chief) conducts research at applied and basic levels leading to: (1) The development of neural control of external devices, i.e., outward information transfer; through the use of normal and abnormal effector organs; through detection of peripheral motor nerve fiber activity; through detection of activity of other central nervous system neurons. (2) Studies leading to the development of external control of the central nervous system, i.e., inward information transfer; through stimulation of normal and abnormal sensory pathways; through electrodes on sensory nerve pathways; through electrodes in the central nervous system. (3) Research leading to the development of neural modeling for the purpose of studying mechanisms of information processing in the central nervous system.

Applicants for Research or Staff Associate positions in the Laboratory should have special qualifications in neurophysiology, the physical sciences, mathematics, engineering or computer technology. Research experience under the guidance of an established investigator is desirable.

The Laboratory of Perinatal Physiology (R. E. Myers, M.D., Ph. D., and staff), functions within the basic neurological disciplines. Areas of specific involvement follow: (1) *Experimental Neuropathology* utilizes biochemical cardiovascular and descriptive neuropathological approaches to explore the patterning and pathogenesis of anoxic brain damage and cerebral palsy. (2) *Physiological Psychology* is concerned with the identification and characterization of neural mechanisms underlying such psychological functions as perception, memory and learning. (3) *Experimental Social Behavior*—Investigates experimental and neural bases of primate social and instinctual behavior. (4) *Developmental Neurology*—The dated monkey pregnancy program within the Laboratory enables studies within the broad area of development utilizing techniques of morphology, physiology or biochemistry.

Collaborative and Field Research Program

Eldon L. Eagles, M.D., Acting Director

In this area, the major responsibilities of scientists are planning and carrying out organized or targeted research programs, particularly in such areas as head injury, epilepsy, and neurological disorders of childhood, and in epidemiological and biostatistical studies investigating causes and contingent factors affecting the rates of various neurological disorders, including impairments or malfunctioning of sensory disorders.

The Slow Virus Studies, under the direction of Dr. D. Carleton Gajdusek, comprise studies of child growth and development and temperate virus infections of the central nervous system. Much of the program derives from the study of the disease kuru and similar subacute degenerative disorders which have successfully been transmitted to the chimpanzee. The child growth study involves all aspects of cultural and physical anthropology of native people in relation to their environment, as well as repeated medical, genetic, and microbiological examination of intensively studied groups. Special research films are being prepared on many aspects of these primitive groups.

The Section on Head Injury, under Dr. J. Kiffin Penry, plans, develops and conducts collaborative and targeted research on various aspects of cranio-cerebral trauma. Of current interest are investigations clarifying the current incidence and prevalence of head injuries; studies of the physical forces of injury, and the simulation of those forces using physical or mathematical models; organized research to elucidate the causes of physiological and biochemical changes which occur with injury is anticipated.

The Section on Epilepsy, under Dr. J. Kiffin Penry, coordinates and conducts collaborative studies of the problem to identify the consequences associated with, or deevloping from this disorder; evaluates the means and the extent to which the course of the disease can be altered; investigates the role of etiological factors, taken singly and in association with each other; appraises and improves the definition and classification of the disorder; along with these studies conducts research to improve diagnostic and therapeutic techniques. A major effort is directed toward developing and testing new drugs for the treatment of epilepsy.

The Epidemiology Branch, under Dr. Jacob A. Brody, has laboratory facilities, a Section on Genetics in Epidemiology, and a research center in Guam. Diseases being studied epidemiologically include multiple sclerosis, neurological syndromes and lung cancer, measles and subsequent neurological and psychological abnormalities, and amyotrophic lateral sclerosis. Major effort in genetics has been a study of dystonia musculorum deformans.

Studies on Guam include ALS and PD, including epidemiological and genetic patterns and clinical and neuropathological studies.

The Perinatal Research Branch (Heinz Berendes, M.D., Chief) directs a program of research concerned with the correlation of factors operating in pregnancy to cerebral palsy, mental retardation and other neurological and sensory disorders of infancy and childhood, and in its own laboratories conducts intensive studies in infectious diseases in pregnancy, using both human and animal populations, and in neuropathology directed primarily to field studies to determine causative factors of brain damage.

The Perinatal Research Branch's Section on Infectious Diseases (John L. Sever, M.D., Head) (1) develops and utilizes large-scale serological methods to study the relation between viral, protozoal, bacterial infections, and birth defects and related abnormalities; (2) conducts investigations on viruses, protozoa, and bacteria, to produce antisera to these agents and to determine the effects of these microorganisms on animals and fetal tissues; (3) investigates recovery of infectious agents and chromosome changes in fetal tissue specimens.

Division of Biologics Standards

Roderick Murray, M.D., Director

The Division of Biologics Standards is accepting applications for Staff Associates in the Laboratory of Bacterial Products, Laboratory of Pathology, and Laboratory of Viral Immunology. Appointments will become effective July 1, 1970 or July 1, 1971, depending on the ability of the laboratories to accept candidates at each time and on the candidates' desires for deferment.

The Laboratory of Bacterial Products (Margaret Pittman, Ph.D., Chief) is engaged in a diversified program of basic and applied research in microbiology and immunology on bacterial vaccines, toxins, and allergens. Emphasis is placed on nature of protective immunological responses, hypersensitivity and toxic reactions and immunochemistry of sensitizing antigens. Preference is given to applicants with pediatric and allergological interest in immunology and hypersensitivity.

The Laboratory of Pathology (Ruth L. Kirschstein, M.D., Chief) is engaged in a program of research in the pathogenesis of infectious diseases, hypersensitivity and immunologic responses with special emphasis on oncogenic viruses and those infectious agents for which there are vaccines and/or other methods of prevention. Animal models of infectious diseases or tumor-producing systems are studied as to the mode of transmission within the colony, spread within each animal, and the final pathologic changes that occur.

Staff Associates will receive extensive training in the pathology of various infectious diseases and animal tumors using the wealth of material accumulated in the last 10 years. In addition, there are opportunities to develop individual research projects in the area of infectious diseases and oncogenesis. Persons interested in such an assignment should have a broad interest in medicine and/or pathology.

The Laboratory of Viral Immunology (Harry M. Meyer, Jr., M.D., Chief) is engaged in programs of virus research with special emphasis on the study of viruses of current or potential importance in the biologics field. Although the laboratory participates in clinical trials of vaccines on occasion, individuals should anticipate spending all or most of their time in laboratory research. Each Staff Associate works under the guidance of a senior

member of the professional staff. Projects vary from basic to applied research depending on the interests of the individual and the needs of the Division. Assignment of this laboratory offers the opportunity to acquire a foundation in laboratory virology and for this reason would be most valuable to physicians planning academic careers in infectious diseases or related fields. The above laboratory gives preference to applicants with 1 or more years of residency training in pediatrics or medicine, but does not require prior experience in virology.

The Clinical Center

Robert M. Farrier, M.D., Acting Director

Robert M. Farrier, M.D., Associate Director

Roger L. Black, M.D., Associate Director

The Clinical Center appoints Clinical Associates for the Departments of Anesthesiology, Diagnostic Radiology, Blood Bank, Clinical Pathology, and Nuclear Medicine. Associates in Anesthesiology and Diagnostic Radiology are expected to have completed their residences prior to entrance on duty.

The ANESTHESIOLOGY DEPARTMENT (Clarence L. Hebert, M.D., Chief) offers advanced training—through the Associate program—to medical graduates who have fulfilled residency requirements of the American Board of Anesthesiology, and who have special interest in research. (Senior residents from other hospitals are accepted for brief periods for special training. Arrangements for such assignments must be made well in advance by the director of the residency program.)

The Anesthesiology Department is organized as a central service to provide anesthesiological care for all patients hospitalized at the Clinical Center, NIH. Inhalation therapy and consultative services for special problems (respiratory, pain, etc.) are included.

Four of the National Institutes of Health have surgical services which have active programs in surgical research.

The National Cancer Institute (Surgery Branch) has a long-range program concerned with the performance of extensive radical surgery with special emphasis on the treatment of patients with malignancy of pelvic organs and structures of the head and neck. In addition, various types of other general surgery are done on NCI patients and those patients sponsored by other Institutes, who require surgery during their Clinical Center stay.

The National Heart Institute admits patients for the study and treatment of congenital and acquired heart disease. All types of cardiac surgery are performed, the majority consisting of open-heart operations performed with the aid of extracorporeal circulation. Six or more of these operations are done weekly.

The National Institute of Neurological Diseases and Stroke has several surgical programs including: localization and surgical removal of epileptogenic foci within the temporal lobe for the treatment of epilepsy; sterotaxic

procedures for the relief of syndromes characterized by abnormal movements and rigidity; and the removal of malignant lesions of the brain with the aid of generalized hypothermia.

The National Institute of Dental Research sponsors a project for the detailed study of physiological variables in ambulatory dental patients undergoing oral surgery under general anesthesia. Various anesthetic agents and techniques are employed in the study. Currently, this study is concerned with the risks involved and the effect of patient position on performance of surgery and patient safety.

The Blood Bank Department (Paul J. Schmidt, M.D., Chief) is accepting applications for Clinical Associateships under the matching system.

The Department supplies over 20,000 blood products annually for transfusion to patients with unique hematologic and immunologic problems. Competent therapy is stressed and clinical programs involving each of the major blood components are in progress.

In addition to its service function, a significant proportion of Blood Bank activity is oriented toward clinical and basic research. As a focal point in patient care and as a repository of diverse blood samples, the Blood Bank provides a unique opportunity for collaborative research with the various Institutes. Current programs in addition to those involving component therapy include investigations into hepatitis and the associated Australia antigen, into the effects of biologic incompatibilities and into the mechanisms of the alteration of cellular antigens by disease states.

The program offers training for the internist or pediatrician in the careful laboratory control of a patient-oriented transfusion program as well as advanced training for the clinical pathologist. A close professional liaison is maintained with the Clinical Pathology Department.

The Clinical Pathology Department (Ernest Cotlove, M.D., Acting Chief) is accepting applications for Clinical Associateships for specialized training and research in areas of cell chemistry, clinical chemistry, clinical microbiology, clinical hematology, erythropoiesis, and computer applications in laboratory medicine. The Department provides all the customary laboratory services and many specialized procedures contributing to the diagnosis, management and study of all research patients in the Clinical Center. The professional staff of the Department are engaged in independent and collaborative investigations in areas relevant to the broad field of laboratory medicine.

The Department is organized in six laboratories (Cell Chemistry, Clinical Chemistry, Clinical Hematology, Clinical Microbiology, Erythropoiesis, and Laboratory Automation and Computer Applications. It is staffed by 123 professional and technical staff, including eight Residents in Clinical Pathology. The laboratories contain advanced automated assay equipment as part of a continuing developmental program in computer-assisted laboratory automation.

Carbohydrate chromatography, amino acid analysis, gas chromatography, radio-immuno-assays, tissue culture, isotope incorporation, cell hybridization, cell separation, nucleic acid hybridization, coagulation factor assays and in-vivo turnover studies are among the many techniques in use in various laboratories of the Department.

Novel approaches to laboratory data processing and interpretation are under study in the Department's own computer facilities. The program for Clinical Associate training offers 2 years of extensive experience in one of the laboratories in the Department. A third and fourth year appointment in the Department may be available to an outstanding Associate as part of a residency training program in academic Clinical Pathology.

The Department of Diagnostic Radiology (Betty E. Hathaway, M.D., Chief) offers a 2-year Clinical Associate program of experience in all phases of diagnostic radiology and advanced training in special study procedures which include: Angiocardiography; femoral arteriography; selective celiac and renal arteriography; inferior venocavography; lymphangiography; carotid and vertebral arteriography; bronchial arteriography; pneumoencephalography and ventriculography; retroperitoneal air studies; sialography; and gynecography.

The Department provides complete diagnostic X-ray services for all of the patients in the Clinical Center. The clinical material studied radiographically is most unusual and many opportunities are available for clinical research.

Approximately 45,000 X-ray examinations are performed annually on 26,500 patients including 2,000 special study procedures.

The Department staff is composed of 10-full-time radiologists, 19 X-ray technicians, two nurses, and 16 accessory personnel.

The professional and physical environment is excellent and close liaison is maintained with the Radiation Therapy Department, the Department of Nuclear Medicine, and the radiology departments of all local hospitals.

The Department of Nuclear Medicine (Jack D. Davidson, M.D., Chief) Each year this Department will accept one Clinical Associate for a 2-year period of training in all aspects of Nuclear Medicine, including limited experience in the therapeutic uses of radioisotopes. Time will be spent among the Department's three sections as well as time available for experience in the Clinical Center Radiopharmacy in which several full-time pharmacists are available for teaching.

The program provides the opportunity to engage in a broad research program in cooperation with the several Institutes at NIH.

Preference will be given to those applicants with training and background in radioisotopes. The specific field of previous residency training is not a primary consideration but one year in approved Internal Medicine, Radiology, or Clinical Pathology is recommended as being in accord with present concepts regarding a future certification in Nuclear Medicine.

The Diagnostic Radioisotope Service performs approximatley 3,000 scans a year utilizing a wide variety of radiopharmaceuticals and both rectilinear scanners and Anger-type scintillation camera. Dynamic function studies are performed as well as experimental studies in conjunction with investigators from other Institutes.

The Radiation Safety Section provides a wide variety of services, including the assay of all radioisotopes for human use. Other responsibilities include accounting for the 80 curies of radioisotopes received and disposed of each year at NIH, performing calibration and safety checks on the 125 X-ray-producing machines and 300 sealed sources, and evaluating over 12,000 film-monitoring badges a year.

The Whole Body Counting Section, with three counter rooms, provides a consultation service to all Institutes and is engaged in basic research on trace quantities of radioactivity, personnel monitoring, and a variety of clinical studies. About 500 whole body counts are performed annually.

PART FOUR

Academic Programs Available to Associates

AMONG the academic programs open to an NIH Associate are: Evening courses provided by the Foundation for Advanced Education in the Sciences, Inc.; formal Seminars under the direction of NIH staff; Combined Clinical Staff Conferences; formal lectures; symposia; and an annual scientific equipment exhibit. The "N.I.H. Calendar of Events" lists an average of 15 to 20 programs each week. Other events of interest are held at universities and other institutions in the Washington-Baltimore area.

Evening Courses

Evening courses are provided by the Graduate Program of the Foundation for Advanced Education in the Sciences, Inc. Established by scientists who subscribe to the view that learning, research, and teaching are mutually reinforcing processes essential to the evolution of science, the Foundation is a non-Federal independent organization as defined by the Government Employees Training Act; however, its tuition and other fees can be paid by a Federal employer. Courses are offered in two semesters, fall and spring; courses are offered at the undergraduate and graduate levels under the programs of its several Departments of instruction: Behavioral and social sciences, biochemistry, chemistry, genetics, mathematics, statistics, physics, medicine and physiology, microbiology and immunology, languages and general studies. Further inquiries regarding the Graduate Program and requests or its current catalog should be directed to: Registrar Foundation for Advanced Education in the Sciences, Inc., National Institutes of Health, Bethesda, Md. 20014.

Seminars

An NIH Program of formal tutorial seminars and informal discussion groups is designed in content and emphasis for prospective independent investigators, and gives them the additional opportunity to master selected topics not adequately covered during college or graduate schooling. These exercises are an integral part of the Associate Program and are geared specifically in that direction. The program accommodates Research, Staff, and Clinical Associates and other properly qualified persons.

A number of tutorial seminars are generally made available each academic year in each of the following categories: biochemistry and genetics; mathematics and physical chemistry; cell biology, immunology and physiology.

Weekly seminars run from September through January and from February through June. Each session is of 2 to 3 hours' duration, and the participants present specific material under the direction of a qualified expert in the field. In preparation for these, the Associate does appropriate outside reading.

Combined Clinical Staff Conferences and Lectureships

Aside from the rounds and staff conferences within the separate Institutes engaged in clinical research, the Clinical Center sponsors at least one monthly Combined Clinical Staff Conference for 9 months of the year. Each conference is conducted by one of the Institute services or an appropriate Department of the Clinical Center. This series of conferences is complemented by Grand Rounds which, in effect, serves the same purpose. The conferences—open to the entire clinical staff and those engaged in laboratory research as well—center around clinical case material having interest for a large portion of the staff, and serve to keep individual investigators abreast of current emphasis in all clinical research.

Several formal lectures are presented annually. The National Institutes of Health Lecture Series was established in 1953 to recognize outstanding scientific accomplishment and to contribute to the interchange of scientific information. The lectureships are awarded by the Director of NIH on the advice of the Scientific Directors of the Institutes. The R. E. Dyer Lectureship was established in 1950 by friends and colleagues of Dr. Rolla E. Dyer, Director of the National Institutes of Health, 1942–50, to pay him tribute upon the occasion of his retirement from the Public Health Service. The award is made at appropriate times—usually on an annual basis—to a scientist who has made an outstanding contribution to knowledge in a field of medical science; and is administered by NIH.

The Jules Freund lecture series was established in 1961 and is presented annually in honor of the first Chief of the Laboratory of Immunology, National Institute of Allergy and Infectious Diseases.

Equipment Exhibit; Symposia

The NIH Research Equipment Exhibit was established in 1951 to acquaint scientists with the most modern research tools and to give them an opportunity to discuss equipment problems with representatives of industry. In 1954, a Symposium on Recent Developments in Research Methods and Instrumentation was added, offering a balanced presentation by specialists in many areas of biomedical research. The two annual events combined to provide a convenient setting for the exchange of information between research investigators and manufacturers of scientific equipment.

The NIH International Symposium on Biomedical Research was established in 1963 to emphasize the mutuality of interest of NIH and the international scientific community, particularly with the extension of NIH programs overseas.

The Washington-Baltimore Educational Complex

The Washington-Baltimore area is widely known for its educational advantages. For example, three medical schools (Howard, Georgetown, and George Washington) are located in the District of Columbia and two (Johns Hopkins and the University of Maryland) are in Baltimore. These and the universities with which they are associated, together with unique institutions such as the Armed Forces Institute of Pathology and the Naval Medical Center, offer exceptional opportunities. Some Associates find the time to pursue a certain amount of formal education at such nearby institutions.

Library Facilities

The National Institutes of Health Library (located in the Clinical Center) provides a central facility for all scientists, technicians, administrators, and supporting staff who are engaged in the research program. As a self-service, open-stack library, it contains a collection of 90,000 volumes and receives 4,500 monographs and 2,800 foreign and domestic journals. Its translation service and the proficiency of its staff in compiling bibliographies are noteworthy.

The National Library of Medicine is located on the NIH campus. While this library serves the entire country, its proximity makes it especially valuable to NIH investigators. Holdings exceed 1 million items—books, journals, theses, pamphlets, prints, and microfilm. Researchers may consult material at the Library and may request printed material through the NIH interlibrary loan service.

Addendum—Residences

Fully approved residency programs are offered in clinical pathology, anatomical pathology, combined clinical and anatomical pathology, and oral pathology and dental public health. Requests for information and application forms regarding these programs should be addressed to the respective program chiefs:

Ernest Cotlove, M.D.
Acting Chief, Clinical Pathology Department
Clinical Center
National Institutes of Health
Bethesda, Md. 20014

Louis B. Thomas, M.D.
Acting Chief, Laboratory of Pathology and
Pathologic Anatomy Branch
National Cancer Institute
National Institutes of Health
Bethesda, Md. 20014

George E. Garrington, D.D.S.
Acting Chief of Oral Medicine and Surgery
National Institute of Dental Research
National Institutes of Health
Bethesda, Md. 20014

Harold Englander, D.D.S., M.P.H.
Chief, Clinical Trials Section
National Institute of Dental Research
National Institutes of Health
Bethesda, Md. 20014

On the basis of agreements between program chiefs and appropriate American Specialty Boards, Clinical Associates in dermatology, psychiatry, and neurology may receive credit for 1 year each. Associates in internal medicine who remain at NIH for a third year may receive credit for this year upon application to the American Board of Internal Medicine.

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